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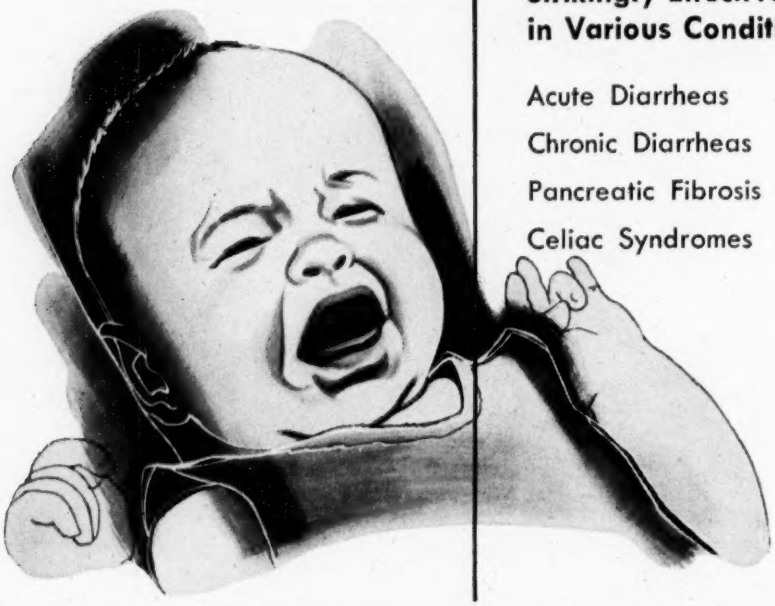

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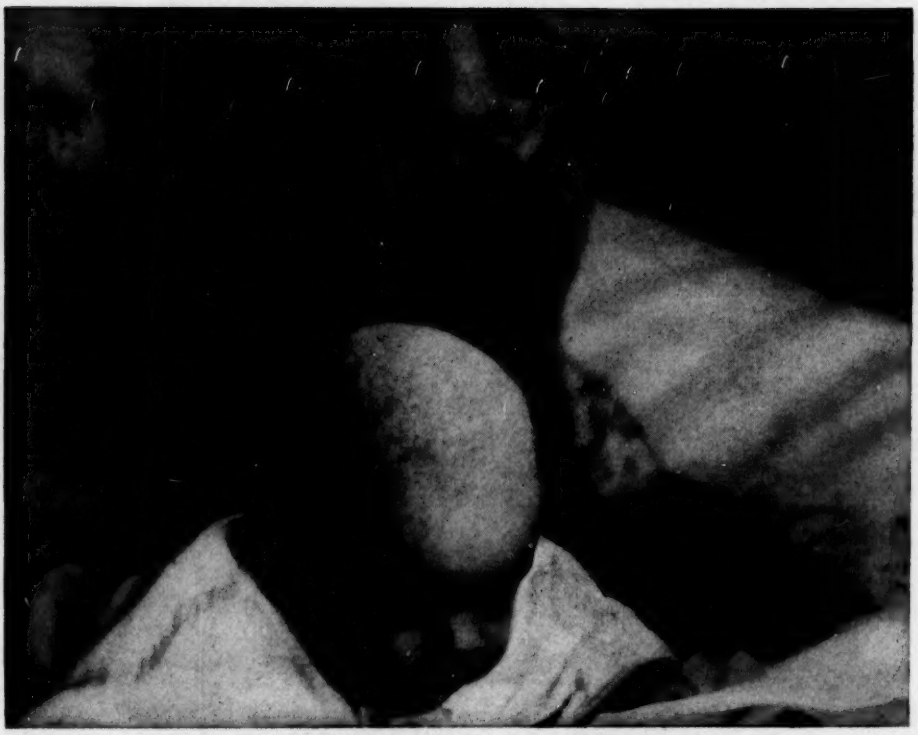

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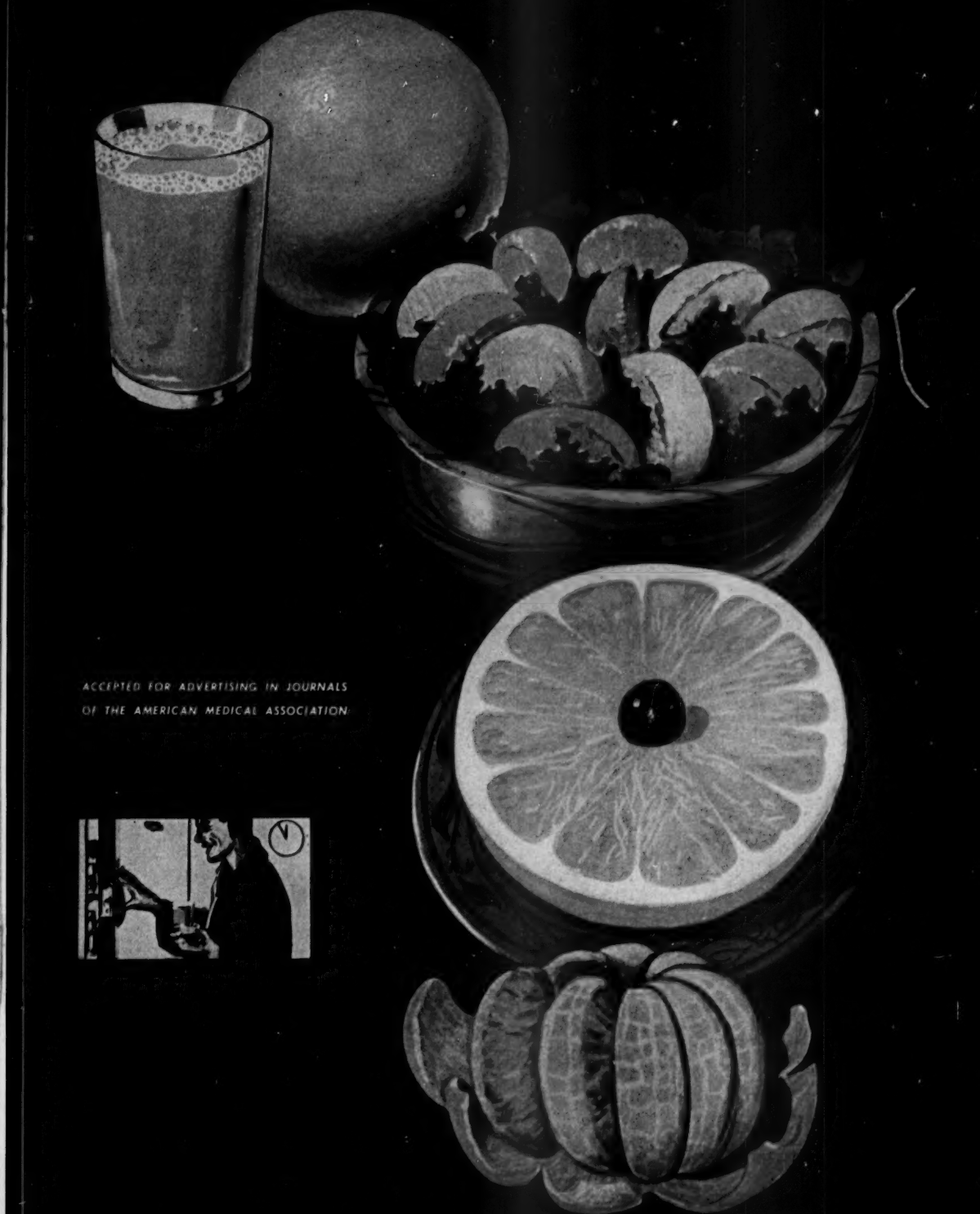

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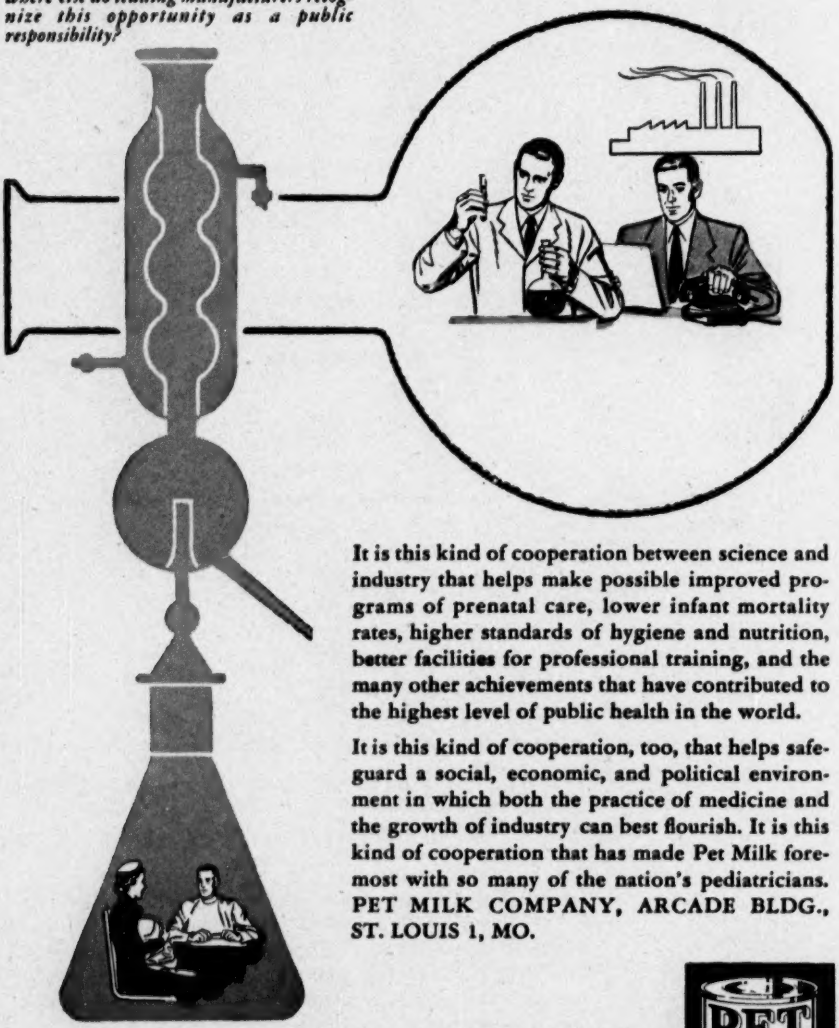

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VOLUME 87 FEBRUARY 1954 NUMBER 2

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TUBERCULOUS MENINGITIS IN INFANTS AND CHILDREN

ARTHUR ROBINSON, M.D.
AND
YOUNG HA RO, M.D.
DENVER

I. INTRODUCTION

THE PAST decade has seen a new and satisfying impetus to the study and treatment of all forms of tuberculosis, but particularly of tuberculous meningitis, a disease heretofore of interest as a diagnostic problem only.[1] However, because of its uniformly fatal outcome, after the establishment of the diagnosis interest in therapeusis was at a low ebb.

Since the advent of new antimicrobial agents against tuberculosis, especially streptomycin, *p*-aminosalicylic acid (PAS), thiazolsulfone (Promizole), and, more recently, isoniazid (isonicotinic acid hydrazide) our attitude toward tuberculous meningitis has become a much more optimistic and positive one. There is no question that the life of a patient with this disease can be prolonged, in many cases for a long period of time. Whether or not these patients are permanently cured, we still do not know. Reports of relapses three to four years after the onset of therapy continue to filter in.

The literature now contains several well-controlled series of cases of tuberculous meningitis treated with varying degrees of success, but all clearly showing that there is still much to be desired in the therapy of this dread disease.*

We wish to add our series of 25 cases of tuberculous meningitis to the literature in order to confirm the findings of other workers and to add certain observations of our own.

One point we should particularly like to stress. Because of the large number of children now being kept alive with various forms of neuromuscular, sensory, emotional, and intellectual damage, the necessity for close cooperation and teamwork among various specialists, such as the pediatrician, neurologist, physiatrist, ophthalmologist, otologist, psychiatrist, psychologist, social worker, and play therapist, has become evident. We hope to emphasize this phase of the therapy in our discussion.

This project was in part supported by United States Public Health Service Grant #E-123 (C_8).

From the National Jewish Hospital and the Pediatric Service, University of Colorado School of Medicine.

Clinical Instructor in Pediatrics, University of Colorado School of Medicine, Attending in Pediatrics, National Jewish Hospital (Dr. Robinson); Fellow in Pediatrics, National Jewish Hospital (Dr. Ro).

* References 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12.

In addition, recent reports on the effectiveness of isoniazid in tuberculous meningitis † have posed the possibility of avoiding the necessity for the intrathecal instillation of streptomycin in these patients, a procedure both painful and not without danger. It seemed justifiable, therefore, to present our experiences with a series of patients, all of whom had received intrathecal streptomycin, since our next series will consist of patients receiving intramuscular streptomycin, PAS, and isoniazid but no intrathecal streptomycin.

II. MATERIAL

This material consists of a series of 25 patients with tuberculous meningitis treated at the National Jewish Hospital between 1948 and 1952. The patients were all children ranging in age from 3 months to 14 years, 18 of whom were under 3 years of age, and 6 of whom were under 1 year of age on admission. Sixteen of these patients were female, an incidence of 64%. The racial background of our cases reflects the racial composition of the lower economic groups of the Rocky Mountain area as follows: Spanish-American, 13; Caucasian, 9; Indians, 2, and Japanese-American, 1.

III. DIAGNOSIS

The following factors were helpful in establishing the diagnosis of tuberculous meningitis in these cases.

A. Positive Tuberculin Test

Twenty-three of our patients, or 92%, had an unequivocally positive test either with 1 : 1,000 dilution of old tuberculin (OT) or purified protein derivative (PPD). Of the two patients with negative tests, one was checked only with PPD No. 1 because a positive gastric smear made the diagnosis definite. This patient may well have had a positive reaction with PPD No. 2. The other patient was in the terminal stage and had a negative OT up to 1 : 1,000. A 1 : 100 OT was not done.

The high incidence of positive skin tests would make us most cautious about diagnosing tuberculous meningitis in any patient with a negative skin test up to 1 : 100 dilution in the absence of bacteriologic evidence of the disease. It is our custom when tuberculous meningitis is suspected in a patient to have the resident immediately give a skin test with a 1 : 1,000 dilution of OT rather than to start with very weak dilutions and work up gradually to more concentrated ones, as is the custom in dealing with other forms of tuberculosis. We feel that an early diagnosis is too important to warrant a more cautious application of the tuberculin test.

B. Spinal Fluid Findings

The majority of patients on admission had the classic findings of elevated protein, lowered sugar, and elevated cell count in a spinal fluid with negative pyogenic cultures. Significant spinal fluid changes on admission were as follows: increased protein, 23 cases (92%); decreased sugar, 16 cases (64%), and increased cells, 24 cases (96%).

Although the spinal fluid chloride level is occasionally lowered on admission, we have stopped doing this determination as a routine, because in every case where it was low the sugar level was also low and in many cases the chloride level was normal on admission.

We have considered spinal fluid sugar levels between 40 and 45 mg. per 100 cc. as normal. It is always necessary in questionable cases to make a simultaneous check

† References 13 and 14.

of the patient's blood sugar, since an abnormal blood sugar level will be reflected in a correspondingly abnormal spinal fluid sugar level. This has occurred in two ways in these patients:

1. Many of these patients have been anorectic and vomiting for several days and may have an abnormally low blood sugar level on the basis of starvation.

2. Some of these patients have received parenteral dextrose to relieve dehydration and acidosis. This may bring an initially low cerebrospinal fluid sugar up to a false normal level, and, unless one is aware of this pitfall, the diagnosis may be missed.

C. Other Evidence of Tuberculosis

1. *Positive X-Ray.*—Only one of these patients had a completely negative chest x-ray. This patient had evidence of tuberculous involvement of the hilar lymph nodes at autopsy.

Of the 24 patients with positive chest x-rays (96%), 6 had miliary tuberculosis, and the rest had evidence of primary pulmonary tuberculosis.

In short, one should be most cautious of the diagnosis of tuberculous meningitis in a child with a normal chest x-ray unless there is other strong evidence for the diagnosis.

2. *Other Nonpulmonary Tuberculous Disease.*—Other nonpulmonary tuberculous disease was present as follows: cervical adenitis, two cases; Pott's disease, three cases, and tuberculosis of the knee, one case.

3. *Contact History.*—Contact history was positive for tuberculosis in 17 cases.

D. Clinical Findings on Admission

Twenty-three of our patients had a clinical picture suggestive of meningitis. The nature and incidence of their symptoms on admission is as follows: fever, 22 patients; stiff neck, 20; vomiting, 18; neurological abnormalities (paresis, abnormal reflexes), 16; irritability and listlessness, 14; diminished sensorium, 9; headache, 7; anorexia, 6; diarrhea, 5, and convulsions, 2.

The two patients without typical symptoms of central nervous system involvement are worthy of further comment. Both of these patients were in the hospital with other forms of tuberculosis and were getting intramuscular streptomycin. Both patients began to show signs of slight irritability and occasionally vomited. Because of our strong index of suspicion, repeated spinal taps were done and an abnormal spinal fluid with positive spinal fluid culture was picked up despite the masking of the typical meningitic findings by intramuscular streptomycin.

E. Bacteriological Findings

Although positive cultures for acid-fast bacilli are not helpful in arriving at an immediate diagnosis, they are necessary for ultimate confirmation of the diagnosis. In 18 of our patients positive spinal fluid cultures for acid-fast bacilli were obtained. Twelve patients had positive gastric cultures; only one patient had a positive urine culture. Six patients had bone marrow cultures, and two of them were positive. In the entire series only two patients have at no time showed bacteriological evidence of infection with tuberculosis. The diagnosis was made in both cases on the basis of positive tuberculin test, positive chest x-ray, and typical spinal fluid findings with a negative spinal fluid culture for pyogens.

In summary, the great majority of children with tuberculous meningitis will have either a positive tuberculin test or a chest x-ray suggestive of tuberculosis or both, and the diagnosis of this condition in the absence of either of these findings should be made most cautiously. History of a tuberculous contact and the presence of extrameningitic forms of tuberculosis are great aids, of course, in the diagnosis.

TABLE 1.—*Twenty-Five Cases of Tuberculous Meningitis*

Patient	Age on Admission	Race	Sensorium on Admission	Associated Pulmonary Findings	Non-pulmonary Tbc. Disease	Period of Follow-Up, Mo.	Present Condition	Neurological Residuals	Mental Retardation
A. S.	8 yr.	S. A.	Coma	Yes	None	39	Good	None	Minor
S. M.	54 mo.	W.	Clear	Yes	None	13	Good	None	None
P. S.	19 mo.	S. A.	Clear	Yes	Cervical lymph-adenitis	17	Good	None	Minor
M. M.	4 mo.	S. A.	Clear	Yes	None	17	Good	Hydro-cephalus	Major
L. J.	10 mo.	W.	Clear	Yes	None	19	Good	Weakness of left hand	Major
R. K.	10 mo.	W.	Clear	Miliary	None	11	Good	None	None
P. D.	34 mo.	W.	Coma	Yes	None	42	Good	Hydro-cephalus	Major
S. C.	24 mo.	W.	Clear	Yes	Pott's disease	63	Good	None	None
M. H. M.	18 mo.	S. A.	Coma	Yes	None	34	Good	Weakness of right leg	Major
R. S.	12 yr.	S. A.	Semicoma	Miliary	None	31	Good	Mild deafness; mild weakness left leg	Minor
C. L.	14 mo.	Indian	Clear	Miliary	None	38	Good	Weakness of extremities	Major
L. D.	18 mo.	S. A.	Clear	Yes	Pott's disease	29	Good	None	Very minor
M. I. M.	17 mo.	S. A.	Clear	Miliary	None	23	Good	None	None
K. A.	3 mo.	S. A.	Clear	Miliary	None	28	Good	None	Minor
J. B.	14 yr.	W.	Clear	Yes	Tbc. of rt. knee	47	Good	Deaf	None
L. A.	28 mo.	S. A	Clear	Yes	Cervical lymph-adenitis	4	Dead	.....	.....
M. T. M.	54 mo.	S. A.	Semicoma	Yes	Pott's disease	1	Dead	.....	.....
D. O.	24 mo.	Jap.	Semicoma	None	None	1	Dead	.....	.....
D. E.	5 mo.	Mex.	Clear	Miliary	None	2	Dead	.....	.....
S. O'c	24 mo.	W.	Coma	Yes	None	2	Dead	.....	.....
S. W.	24 mo.	Indian	Coma	Yes	None	2	Dead	.....	.....
R. A.	48 mo.	W.	Clear	Yes	None	5½	Dead	.....	.....
S. M.	17 mo.	S. A.	Coma	Yes	None	2	Dead	.....	.....
D. H.	7 mo.	W.	Clear	Yes	None	4	Dead	.....	.....
T. V.	7 yr.	S. A.	Clear	Yes	None	3	Dead	.....	.....

IV. TREATMENT

We have attempted to standardize the therapy as much as possible as described below. However, at times, of course, it was necessary to individualize the therapy as situations in particular patients arose, for example, vomiting of PAS and toxic reactions to streptomycin.

A. ANTIMICROBIAL THERAPY

1. *Controlled Study.*—Four patients—J. B., A. S., P. D., L. A. (Table 1)—were part of a nationwide controlled United States Public Health Service study of tuberculous meningitis [11] and were treated with alternate 6-week treatment courses and 10-day rest periods. All the other patients were treated continuously.

2. *Intramuscular Streptomycin Therapy.*—Streptomycin was administered intramuscularly in doses of 100 mg. per kilogram of body weight per day in two divided doses given daily for two weeks. Then 50 mg. per kilogram per day was given daily until about three months after the spinal fluid had become normal.

3. *Intrathecal Streptomycin Therapy.*—Streptomycin was administered intrathecally daily for about 30 instillations or, preferably, until the spinal fluid began to improve. At that time the dose was given every other day until the spinal fluid became normal.

This medication was administered by the lumbar route, except in those patients in whom the spinal fluid protein remained over 100 mg. per 100 cc. In these patients the streptomycin was instilled intracisternally in one-half the amount given by the lumbar route at least twice weekly, it being given by the lumbar route the rest of the week. Eleven of our patients were treated in this fashion, and it may be stated here that although literally hundreds of intracisternal instillations were made, in no case was there a serious reaction. Once the resident staff learned the technique, no difficulty was had, and we have not felt that in our hands it was a particularly dangerous procedure.

Nine patients with definite evidence of block had burr holes performed and had a daily intraventricular instillation of streptomycin in only one-third of the intralumbar dose. Only two of these patients are still alive.

The dosage of intrathecal streptomycin was arbitrarily set as follows: up to 18 months of age, 25 mg.; 18 months to 15 years of age, 50 mg.

When patients evidenced a toxic reaction to the intrathecal streptomycin (vomiting, drowsiness, headache, fever), the dose was cut in half.

4. *Streptokinase and PPD Therapy.*—Streptokinase and PPD were also given occasionally intrathecally in cases of block. The use of these drugs will be discussed later under the heading of "block."

5. *PAS Therapy.*—PAS was given by mouth in doses of 0.2 gm. per kilogram per day, with a maximum dose of 12 gm. per day in three divided portions. The drug is to be given daily by mouth for two years after the discontinuance of streptomycin therapy. It is administered in an elixir of PAS, and is prepared as follows: PAS, 100 gm.; sodium bicarbonate, 60 gm.; methyl salicylate, 5 drops; syrup of cinnamon, 165 cc., and water, to make 500 cc.

With this 20% solution of PAS, most children were able to tolerate the drug well. When a child vomited it, the drug was stopped for a week and was then reinstituted in gradually increasing doses. On discharge, children were sent home with tablets of PAS because of greater durability, the elixir of PAS being stable only for about two weeks. Occasionally a child received sodium PAS subcutaneously when vomiting persisted.

6. *Thiazolsulfone.*—Some of the patients in our earlier cases also received thiazolsulfone in doses of 2 to 3 gm. per day. However, as a result of the nationwide study of tuberculous meningitis under the auspices of the United States Public Health Service,[11] in which alternate patients were treated with PAS and thiazolsulfone while the other half were treated with PAS alone and in which there was no difference in the results obtained with the two groups, we are no longer administering thiazolsulfone.

7. Isoniazid.—Five of our most recent patients, S. M., R. K., O. J., M. M., and P. S. (Table 1), who were not thought to be doing well were given in addition to the above treatment isoniazid in a dose of 10 mg. per kilogram per day for 10 days and then 4 mg. per kilogram per day by mouth. All of these patients seemed to improve, especially as regards the spinal fluid findings, after the administration of this drug.

B. Supportive Care

This should be stressed especially during the early days of the disease. This consists of free use of supportive blood transfusions and parenteral fluids with particular attention to electrolyte balance in the smaller patients. A high-protein high-calory high-vitamin diet is administered. In this connection expert and enthusiastic nursing care is vital, as some of these children require the greatest patience in being fed. Many of them, of course, need gavage feedings during the initial month or two of therapy.

C. Physical Therapy

As more and more of these patients have stayed alive, we have found it most important to have a concentrated course of physical therapy started early and carried throughout the period of hospitalization and, when possible, after hospitalization. This therapy is under the direct supervision of a qualified physiatrist and will be discussed more later on.

D. Psychotherapy

Psychotherapy is another vital part of the treatment program. A qualified play therapist and a psychologist work with the children under the direction of a psychiatrist.

V. FOLLOW-UP

The majority of these patients were given routine special monthy examinations during their period of hospitalization which included electroencephalographic, ophthalmologic, psychologic, and physiatric studies. The results of these special examinations will be discussed later.

VI. RESULTS

A. Survival

Fifteen of the 25 patients have been alive for at least six months, a survival rate of 60% (Table 1). In a breakdown according to age, the following results are apparent: Under 3 years of age there were 18 patients; of these eight have died, giving a survival rate of 56%. Under one year of age there were six patients; of these two have died, giving a survival rate of 66⅔%. Under 2 years of age there were 15 patients; of these 6 have died, giving a survival rate of 60%.

VII. PROGNOSIS

If our mortality figures are correlated with the interval from the onset of symptoms to the onset of treatment (Table 2) it will be seen that in our cases there is no significant difference between the results obtained in those patients treated soon after the onset of symptoms, and those in the patients treated later. This may mean only that those treated earlier had a severer degree of meningitis which therefore gave obvious symptoms sooner and so allowed the diagnosis to be arrived at sooner.

If the mortality figures are correlated with the condition of the patients on admission (Table 3), it is evident that only those patients who were admitted with

a clear sensorium had a good prognosis. In our series, the mortality rate in this group has been 32%. In addition, only two out of the 11 survivors in this group showed evidence of severe neurological damage.

If our mortality figures are correlated with the presence or absence in these children of associated pulmonary lesions (Table 4) it will be seen that the prognosis

TABLE 2.—*Mortality According to Interval Between Onset and Treatment*

Interval	Total		Alive		Neurologic Damage of Those Alive, by Age	
	<3 Yr.	>3 Yr.	<3 Yr.	>3 Yr.	<3 Yr.	>3 Yr.
Less than 2 wk	10	3	6	2	5	1
Between 2 and 4 wk	6	4	3	2	0	0
Over 4 wk	2	0	2	0	0	0

TABLE 3.—*Mortality According to Sensorium on Admission*

Sensorium on Admission	Total		Alive More Than 6 Mo.		Alive with Severe Neurologic Damage	
	<3 Yr.	>3 Yr.	<3 Yr.	>3 Yr.	<3 Yr.	>3 Yr.
Clear	12	4	9	2	2	0
Semicoma	2	2	0	1	0	0
Coma	4	1	2	1	2	0

TABLE 4.—*Mortality According to Presence of Associated Pulmonary Lesion*

	Total	Under 3 Yr.	Over 3 Yr.	Mortality Rate, %
	24	17	7	
Alive	15	11	4	37
Total number with miliary lesions	6	5	1	
Alive	5	4	1	17
Total number with pulmonary lesions other than miliary	18	12	6	
Alive	11	8	3	38

TABLE 5.—*Relation of Initial C. S. F. Protein to Prognosis*

	Total No. Cases	Dead
Initial protein over 100 mg./100 cc.	11	8
Initial protein under 100 mg./100 cc.	14	2

of the child with miliary tuberculosis and tuberculous meningitis is certainly no worse than that of the child with tuberculous meningitis alone. In fact, it has been our feeling that perhaps he does a little better. This impression may have theoretical support if one considers that the child with miliary tuberculosis and meningitis is suffering from an acute hematogenous disease presumably more susceptible to antimicrobial therapy, while the child with meningitis alone may have developed it as a result of a perifocal spread of an older tuberculoma, presumably less susceptible to therapy.

In Table 5 the outcome of the disease has been correlated with the initial level of spinal fluid protein, and it is evident that the prognosis is much better in those patients with initial level below 100 mg. per 100 cc.

VIII. COURSE IN HOSPITAL

As is shown by Table 6, all components of the spinal fluid began to improve between the second and fourth months in the average patient who did well, and the spinal fluid became normal between the seventh and eighth months, with the sugar level usually becoming normal first and the protein level becoming normal last.

TABLE 6.—*Improvement of C. S. F.*

Patient	Time of First Improvement of C. S. F., Mo.			C. S. F. Became Normal, Mo.
	Cells	Prot.	Sugar	
R. K.	4	4	3½	7
L. J.	2	3	3	7
P. S.	1½	1½	1	6
M. M.	3	3	2	6
S. M.	3	3	1	9
L. D.	2	3½	3½	7
C. L.	4	5	3	8
R. S.	2	3	3	11
K. A.	2	3	4	8
A. S.	2	3	1½	10
I. M.	½	3	½	9
M. H. M.	1	2	2	10
S. C.	1	3	2	4½
P. D.	3	4	2	8
J. B.	2	4	2	10

TABLE 7.—*Eye Findings in Twenty-Five Children with Tuberculous Meningitis*

	No. Patients	Alive	Dead
Normal fundi	10 (40%)	8	2
Optic atrophy	4	2	2
Optic neuritis	2	1	1
Retinal exudate	1	0	1
Pallor of optic nerve	3	2	1
Papilledema	2	2	0
Choroidal tubercles	4	3	1

The average patient was febrile on admission and became afebrile in a period of one to three months, except for those who had some complication such as a severe lymphohematogenous spread (P. S.). The average patient began to gain weight in two to three months.

Those patients who on admission were stuporous and who improved became alert in periods varying from two weeks to as long as three months.

A. EYE FINDINGS

All patients have had complete eye examinations at monthly intervals by a qualified ophthalmologist.‡ There were positive findings in 11 of the 25 patients (Table 7). Although some of these findings, particularly the presence of choroidal

‡ Dr. Eli Bard.

tubercles, are helpful in establishing a diagnosis, and although we have been surprised at the frequency of positive eye findings if they are looked for in this condition, we have been unable to use any abnormal eye findings as a prognostic aid.

B. Neurological Residua

Of the 15 patients still alive, 4 show evidence of severe neurological damage. Three of these patients were comatose on admission. The fourth patient had a clear sensorium on admission but had a left hemiparesis. She developed progressive signs of block and for this reason received intraventricular PPD. During the course of this therapy she had high fever, vomiting, and convulsions. The signs of block disappeared during treatment, but the hemiparesis persisted. At present she shows evidence of severe mental retardation. Whether or not this is due to the administration of PPD, we do not know.

Three other patients have minor neurological changes in muscle strength and reflexes of a unilateral nature.

Many of the patients show some degree of mental retardation, five of them very severely. The amount of ultimate retardation of the others will have to await further follow-up, as many of these are showing persistent improvement.

Since infants and young children with tuberculous meningitis must be hospitalized for long periods, they are deprived of the motherly warmth and affection which is so necessary for normal emotional and mental development during this period. In addition, the traumatic nature of the therapy is such as to prevent further the progress of emotional and mental development.

Approximately two years ago the position of play supervisor was created in order to provide the children with a person who would give no medical treatment, but who would be a steady and dependable source of affection. The play supervisor provides a stimulating environment by taking all those who need not be bedfast, including children as young as one year, to a carefully equipped playroom where they can participate in a modified nursery school program for an hour each day. She visits with those children whose medical condition militates against this activity, utilizing phonograph records and toys. She sees that a supply of the latter is kept within reach of the patients at all times.

A major problem in the treatment of a child with tuberculous meningitis has, of course, been the diagnosis of mental deterioration. The problem is made complex because of depressive states developed by infants and young children as a result of long hospitalization. This condition, referred to by Spitz as "hospitalism," [15] can cause a child who has suffered no actual brain damage to become and to remain intellectually and emotionally retarded. Of six apparently markedly retarded patients, all in the first three years of life, three were restored to a state of normal functioning following a period of concentrated affection given by the play supervisor. During this time the children were fondled, caressed, carried about, rocked, and sung to daily. The three whose behavior and level of activity remained unchanged were also those with signs of the severest neurological damage and could thus be said to have had severe brain damage affecting their mental ability as well as their locomotion and coordination.

In an attempt to quantitate the total effect of these factors, 13 patients have been checked with psychological tests. It is our hope to follow them over a period of years with repeated examinations in order to see how much of this damage can

be repaired. By concentrating on minimizing the effects of separation from home and institutionalization by the use of a mother figure, we hope to diminish as much as possible all extraneous factors and be left only with the effects of brain damage.

These children were tested with the Vineland Social Maturity Scale and the Psyche Cattell Infant Intelligence Scale. It should be stressed that practically nothing is known about the psychological background of these cases. This is an inherent defect in attempting to evaluate present functioning or in attempting to predict future rate of development. Thus far, however, the following genalizations may be made:

1. All children were retarded in the intellectual and socialized areas, some very much more so than others.

2. All children showed some initial fear of the examiner, which associated him with the therapy.

3. All children evidenced a warm recognition of the play therapist, the mother figure, and seemed anxious to learn new things in order to please her.

C. Electroencephalographic Studies §

Nine patients were followed electroencephalographically at monthly intervals. The details of this study will be the subject of a future communication. Suffice it to say here that from the studies we feel that the following conclusions are justified:

1. The use of intracisternal and intrathecal streptomycin produces no permanent adverse effects on the electroencephalogram. Any changes that may be related to the administration of streptomycin are reversible and are more likely to appear in a previously disturbed brain wave patient.

2. Intracisternal streptomycin did not alter a normal electroencephalogram.

D. Recurrences

We have not yet been troubled with the problem of recurrence or relapse, except in one of our original patients (J. B.), who by our present standards would be considered to have been undertreated. This patient was originally treated for only three months with intrathecal and intramuscular streptomycin. Six weeks after therapy was stopped, she had a definite recurrence of disease with abnormalities of the spinal fluid and the recovery again of tubercle bacilli from the spinal fluid. She responded promptly to further therapy and has since done well. We compare our experience with the above-described therapy with that of another patient under our care, but not included in this series. This 4-year-old girl received intramuscular therapy alone for five months at another hospital and improved greatly. She then had a relapse and went into a coma, developed block, and recently died.

At the time of this writing however, two of our more recent patients, R. K. (in this series) and E. W. (not in this series), developed a sudden pleocytosis and a slight change of spinal fluid chemistries. This was associated with a rise of temperature to 102 F. These abnormalities lasted for only a few days, and the return to normal was effected with no change in treatment. R. K. had had six months of intrathecal therapy, one month of intramuscular streptomycin alone, and isoniazid. Intrathecal therapy had been stopped at six months because he seemed to be getting severe headaches from the intrathecal instillations and because the spinal fluid was

§ Obtained with the cooperation and help of Dr. E. W. Busse, Director of Division, Psychosomatic Medicine, University of Colorado School of Medicine.

normal. E. W. was still getting intrathecal streptomycin when the complications occurred. We have no explanations for these two occurrences, both new in our experience, and at present do not feel that they can be considered true relapses. At the time when these children developed these findings, many of the other patients on the ward were suffering from a "flu-like" syndrome, and it is possible that these patients had a mild encephalitis unrelated to tuberculosis.

E. Hydrocephalus

Four patients in the group of survivors developed definite hydrocephalus as shown either by a rapidly growing head (three children) or by a positive pneumoencephalogram (one patient). However, of the 10 patients who died, 8 were autopsied and, of these, 6 had hydrocephalus, 2 only slightly. The two without hydrocephalus died within three weeks of the onset of symptoms.

F. Block

The problem of block in the circulation of the spinal fluid is still a difficult one to resolve. We have taken as evidence for a developing block the following findings:

Table 8.—*Treatment with Streptokinase and Streptodornase*

Dosage.....	10,000 U. S-K in 2 cc. Sol.
Methods.....	Remove 10 cc. of C. S. F. Instill 2 cc. S-K and 3 cc. C. S. F. This is done twice weekly
Reaction to treatment.....	Increased intracranial pressure Spinal fluid changes A. Cells rise B. Protein rise } In 24 hr. C. Sugar falls Clinical symptoms: Meningismus, headache, high fever Vomiting within 4-24 hr.

(1) rising spinal fluid protein; (2) marked difference between the level of protein in the lumbar spinal fluid and the cisternal fluid, or the ventricular fluid, and (3) developing hydrocephalus. (We are not sure that the assumption of a developing block is justified on the sole evidence of hydrocephalus.)

Many methods have been proposed for the prevention of a block or for the destruction of one after it has occurred. We have tried the folowing methods: (1) intracisternal or intraventricular instillation of streptomycin several times a week when the spinal fluid proteins persisted over 100 mg. per 100 cc. (11 patients); (2) intrathecal instillation of streptokinase (four patients); (3) intrathecal instillation of PPD (seven patients); (4) surgical incision of adhesions at the base of the brain (one patient).

Of all these methods, the first, namely, the intracisternal or intraventricular instillation of streptomycin, has seemed the most helpful. Five of the patients who are still surviving received intracisternal or intraventricular instillations of streptomycin because of a persistently rising spinal fluid protein. In these patients the trend toward a rise in protein was reversed. Of course, we cannot say that the reversal of this trend was due to the intracisternal or intraventricular instillation of streptomycin, although we suspect as much.

Four patients received repeated instillations of streptokinase [16] (Table 8). Very severe reactions resulted, and, despite the drug, all the patients died.

The intrathecal instillation of PPD for the purpose of breaking up beginning block formation, as proposed by Smith and Vollum,[17] was performed on seven cases in which we felt block was developing.|| The results were not at all impressive. In two

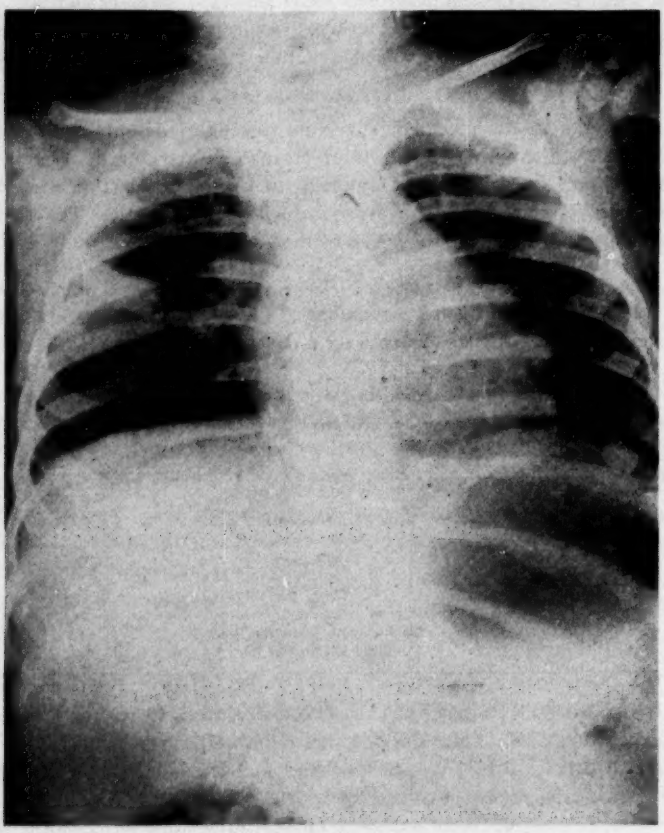

Fig. 1.—Chest x-ray of L. J. Sept. 17, 1952.

|| Taken from Smith and Vollum.[17]

"On admission 0.1 ml. o. T. 1/1000 is injected intradermally. Then, as soon as the diagnosis is confirmed, bifrontal burrholes are made if this has not already been done. A 'standard' solution of P.P.D. is made up containing 7.5μg. per ml. and this is further diluted 10-fold, 100-fold, and 1000-fold. If the Mantoux test is strongly positive, then 0.5 ml. of the 1000-fold dilution is injected intrathecally and this amount is doubled every other day until a reaction is obtained.

"If the Mantoux is weakly positive to O.T. 1/1000 or more, then 1.0 ml. of the 1000-fold dilution is injected and the dose is at first trebled or even quadrupled every other day, depending on the strength of the Mantoux reaction. When we are giving 0.5 ml. of the 100-fold dilution we increase the dose more cautiously in order to avoid too severe a reaction.

"Once a reaction is obtained, as shown either clinically or by a rise of the cells and protein in the C.S.F., the same dose is repeated. From then on the size and timing of each injection is decided on according to the severity of the last reaction. On the whole it has seemed wiser to give the injections every third or fourth day so as to allow two or three days free from fever and vomiting. The dose is gradually increased as the patient becomes more tolerant of the injections."

cases no response at all was obtained with large doses of material. Three cases gave good reactions of the type described by Smith. Of these, one, L. J., seemed to be definitely better after each reaction. This patient, and one other, M. M., are the only ones who received PPD and are still alive. M. M. did not seem to be helped by it.

Because of the lack of typical response to PPD (Sharp & Dohme, Inc.) both clinically and by laboratory examination, some Weybridge PPD was obtained from

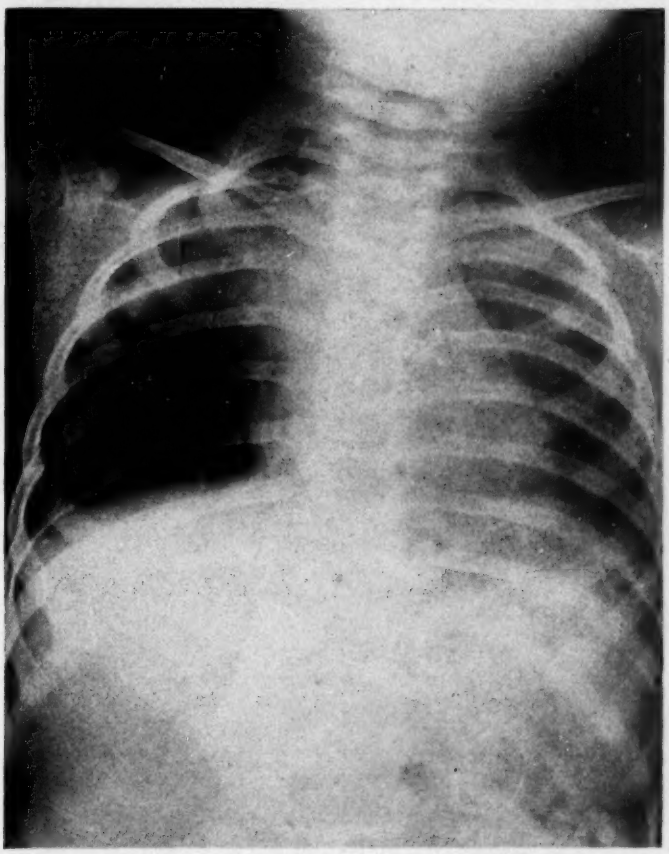

Fig. 2.—Chest x-ray of L. J. Jan. 17, 1952.

England through the help of Dr. Gardner Middlebrook. This material was tried on three patients with no different results.

Extremely severe reactions, including fever and convulsions, were obtained after use of PPD on three patients, one of whom, S. W., died in a reaction. It should be added that all these patients have burr holes placed prior to the onset of PPD therapy and received ventricular taps at the time of a reaction.

It is interesting to note that one patient, L. J., seemed to have developed a spread of her pulmonary tuberculosis while on PPD therapy (Figs 1, 2, and 3). That this spread was probably of an allergic nature is evidenced by its rapid clearing without change in treatment.

In summary, then, our results with PPD have not impressed us with its efficacy in breaking up a block. We realize, however, that we may have been too conservative in waiting until definite evidence of a block was present before using the material and that perhaps in the future the PPD instillation should be performed much earlier in the patient's course. Also, we are sure that we have been too cautious in increasing the dose of PPD in an attempt to find the correct dosage to cause a reaction. In the

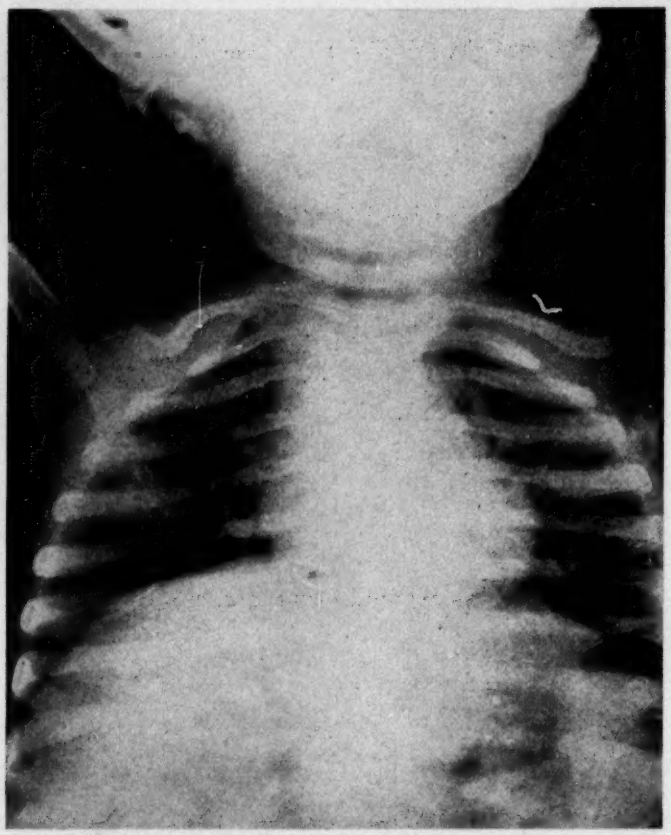

Fig. 3.—Chest x-ray of L. J. Feb. 8, 1952.

future we will increase the dose much more rapidly than Smith recommends. In this way it will not take so long to reach an effective dose (often 1 mg. of PPD), and one is not so likely to desensitize the patient to tuberculin in the process.

G. Physiatric Care¶

The treatment of the child with neural involvement as a result of tuberculous meningitis may be approached from three angles: first, the prevention of local changes; second, the development of residual function in the muscles, and third, the facilitation of development of secondary neural pathways.

¶ Contributed by Dr. Jerome Gersten, University of Colorado School of Medicine.

As a result of increased tone of elbow, wrist, and finger flexors, shoulder and arm adductors, and plantar flexors, there are periarthritic changes in the involved joints and eventually contracture and fibrosis of the involved muscles. These changes must be prevented or minimized, for full recovery from the neural standpoint would be of no avail in the presence of an end organ which could not respond. The joint fixation can be prevented by passive motion of the joint through full range for at least one period each day. Five to 10 such passive movements during each period will be adequate. The changes in muscle structure and function are not so easily remedied. Fortunately, the irreversible phenomenon of fibrosis can be minimized by the same passive movements used for prevention of joint fixation. The functional changes which accompany contracture and muscle disuse and which include changes in muscle weight, potassium, adenosinetriphosphate, and myosin are effectively restored toward normal only by active movements of the muscle.

Thus, the development of residual function in muscles depends upon the institution of active exercises. In the adult and older child the antagonists of the spastic muscle receive most attention, with the finger, wrist, and elbow extensors and the dorsiflexors of the foot working against as much resistance as possible. In the infant and younger child this specific approach has to be ignored and the third phase emphasized. Movement patterns which emphasize the antagonists of the spastic muscle groups are encouraged. This can usually be approached only through a play environment.

C. Postmortem Findings

Postmortem findings on these patients were not remarkable and have been adequately described in the papers of Denst, Winters, and others.# The streptokinase-treated patients did not have any unusual findings post mortem, except for one who had an unusually severe leptomeningitis, fibrous and nonspecific, over the convexity of the brain.

The PPD-treated cases, who were autopsied, were also not remarkable in the amount of tuberculous reaction at the base of the brain, if compared with the non-PPD-treated cases.

In many of the patients with healed tuberculous lesions in the brain, there was still evidence of progressive primary infection in the lung, another example of a well-known, but still interesting, observation, namely, that tuberculosis can be healing in one organ of the body and simultaneously be spreading in another.

COMMENT

This paper emphasizes the fact, mentioned at the outset, that although tremendous strides have been made in the treatment of tuberculous meningitis, great advances still have to be made before it can be considered to be adequate. We feel that the most hopeful approach is undoubtedly that of prevention of this dread disease, particularly with the use of BCG. We are impressed by the statement of Arvid Wallgren [21] to the effect that he has not observed a case of tuberculous meningitis in Scandinavia in an infant adequately vaccinated with BCG.

Hope has been held out by others * that the addition of a potent antimicrobial agent such as isoniazid to the therapy may improve the outlook, particularly insofar

References 18, 19, and 20.

* References 13 and 14.

as making unnecessary the intrathecal instillation of streptomycin. So far we are treating six cases with isoniazid and no intrathecal streptomycin (not in this series), and our results do not seem to be much different. Another subject to be investigated is the possible advantage and increased efficacy of the PPD therapy in the presence of isoniazid administration, since isoniazid has been shown to be most effective against the rapidly multiplying tubercle bacilli,[22] and since PPD may increase the rapidity of multiplication of the tubercle bacilli.

We should also like to emphasize our observation that in our experience miliary tuberculosis combined with tuberculous meningitis is no more serious in prognosis than meningitis itself. In fact, the reverse may be true. We stress that this is true in children, and do not doubt reports to the contrary which are based on adult patients.[8]

The electroencephalographic findings are again worthy of mention in that they at least do not lend credence to the fears of many that intrathecal streptomycin itself may be harmful.

Finally, we feel that enough stress in the past has not been placed upon the necessity for teamwork, including many specialties in the follow-up of the surviving patients, which, needless to say, should continue for many years. Particular attention should be paid by the physiatrist, speech therapist, psychologist, and social worker to the care of these patients.

SUMMARY

Twenty-five cases of tuberculous meningitis in children are presented. Treatment and results are discussed.

Emphasis is placed on the necessity for teamwork in many specialties for the care and following of these patients.

Methods of combating block with and without streptokinase and PPD are described.

The inadequacy of present-day therapy is discussed.

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ARACHNODACTYLY ASSOCIATED WITH ANEURYSM OF THE AORTA

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THERE have been numerous reports in the literature of arachnodactyly, but there are only a few cases reported in which there was an associated aortic aneurysm. Of over 300 cases of arachnodactyly (or Marfan's syndrome) in the literature, relatively few autopsy reports can be found. Marvel and Genovese [1] reported a case of Marfan's syndrome with medionecrosis of the aorta and aneurysm formation in a 29-year-old Negro man (this is the 29th case). They also presented an excellent summary of the previous cases with autopsies reported in the American literature.* In 26 of the 29 cases they reviewed there were heart lesions. At 16 of the 26 autopsies aortic aneurysms were found, in 12 of which instances medionecrosis of Erdheim [8] was described. Half of the persons with aortic aneurysm were men, and half were women. The youngest patient was a 14-year-old girl, and the oldest was a 52-year-old woman. The remaining 14 patients were between 21 and 35 years of age, 12 being in their twenties.

Goyette and Palmer [9] reported a case of arachnodactyly in a 23-year-old Army corporal who suddenly died. Postmortem findings were those of a dissecting aneurysm throughout the entire aorta, extending into the innominate artery, the left common carotid artery, the left subclavian artery, and each common iliac artery. Medionecrosis of Erdheim was present. Thomas and associates [10] reported three cases of aortic aneurysm associated with arachnodactyly. Two Negro men aged 32 and 26 years, respectively, died of this condition. Autopsy revealed medionecrosis of Erdheim of the aorta in each case. A 35-year-old sister of the latter patient was alive and had clinical evidence of arachnodactyly and aneurysm of the aorta.

We are presenting two cases of arachnodactyly associated with aortic aneurysm occurring in a 9-month-old boy and a 10-year-old boy. To our knowledge, this condition has never before been described in an infant. This infant also had all the major and minor manifestations of a true Marfan's syndrome, including dislocation of the lens of the eye.

REPORT OF CASES

CASE 1. (Fig. 1).—H. O., a 9-month-old white boy, entered the Children's Memorial Hospital on Aug. 4, 1950, because of a "cough and cold" which had been present for three days. Three weeks prior to admission, the patient was treated elsewhere with penicillin and chlortetracycline (Aureomycin) for a cough. X-ray studies at that time revealed "an enlarged heart or tumor of the lungs." Because of that possibility he was seen as an outpatient by Dr. Stanley Gibson on

From the Children's Memorial Hospital and the Otho S. A. Sprague Memorial Institute Laboratories.

* References 2, 3, 4, 5, 6, and 7.

July 24, 1950. When he returned for further study on Aug. 4, there was marked respiratory distress. There had been anorexia and occasional vomiting, but no hemoptysis. The cough was productive of mucus.

Birth and feeding history had been normal. The boy had smiled at 1 month of age and had cut his first tooth at 6 months of age. He did not sit up. An inguinal herniorrhaphy was performed on alternate sides at 3½ and 7 months of age, respectively. The family history was noncontributory.

Physical examination was as follows: He measured 84 cm. (33.4 in.) and weighed 7.2 kg. (15.8 lb.). The chest diameter was 37.8 cm. (14.8 in.) and the head diameter was 44.5 cm. (17.5 in.). The anterior fontanel was closed with a prominence of the suture lines. There was a prominence of the frontal bones and supraorbital ridges. A receding chin was evident, as were thin lips and a narrow high palate. The left lower central incisor had erupted, and the right upper central incisor was erupting. There was marked fibrillation of the tongue. Ophthalmological consultation reported that the eyes were large with small regular pupils which reacted to light and accommodation. The lens was normal on the left, but dislocated downward and medially on the right. There was neither nystagmus nor strabismus present. The ears were large, and only soft cartilage was present. The neck was supple, and small anterior and posterior cervical nodes were palpated.

On examination of the chest there was noted a thin chest wall and dullness on percussion over the right side posteriorly. Moist crepitant rales were heard over this area. Between the scapulae, bronchial breathing was heard. The heart was enlarged one fingerbreadth to the right and left. A Grade-IV harsh systolic murmur was heard at the apex in the fourth and fifth left interspaces, being transmitted over the back and to the left anterior axillary line. Femoral pulsations were present. The blood pressure was 84/60 mm. of Hg.

The abdomen, genitalia, and rectum were normal. Well-healed inguinal herniorrhaphy scars were present.

The extremities were very weak, with flabby musculature. There was an absence of the deep reflexes. The fingers, toes, and general skeleton were long and thin. Contractures of the fifth fingers were noted. The infant had the appearance of an Oppenheim's disease and Werdnig-Hoffmann disease, with arachnodactyly and arthrogryposis.

The laboratory data were as follows: hemoglobin 8.1 gm. per 100 cc.; red blood cells, 3,860,000, with hypochromia and microcytosis; white blood cells 11,000, with 28% polymorphonuclear leucocytes, 68% lymphocytes, and 4% monocytes. The findings on urine analysis were negative.

The electrocardiogram was within normal limits. A shadow overlying the heart was seen upon chest film and fluoroscopy. It appeared that the right ventricle extended forward from the denser shadow. No specific type of congenital heart disease was seen on angiocardiography. The heart enlargement was largely confined to the right auricle and right ventricle.

The patient did well on antibiotic therapy and was discharged Sept. 1, 1950.

On Sept. 7, 1950, he was readmitted to the hospital with a four-day history of anorexia, cough, fever, and lassitude. Physical examination at this time was essentially the same as before, plus a severe bilateral pneumonia, dehydration, and toxicity. The child appeared in extremis.

Intracardiac epinephrine, oxygen, penicillin, nikethamide (Coramine), and caffeine were administered. The patient died 30 minutes after admission.

Pathological Summary.—The autopsy was performed five hours after death. The body was that of a poorly nourished flabby white boy 10 months of age, measuring 84 cm. in length and weighing 7.2 kg. Externally, the body conformed to the description given in the physical examination. Through a primary Y-shaped incision the chest and abdomen were opened. There was almost no subcutaneous fat. The heart was enlarged, weighing 190 gm. (normal 39 gm.) and causing a complete atelectasis of the left lower lobe of the lung. When the heart was opened, the most striking abnormality was the peculiar serrated border of the mitral and tricuspid valves, with thickening along the free border and with a chorda tendineae attached to the center of each serration. There was a marked aneurysmal dilatation of the ascending aorta, with a high origin of the coronary ostia. The aorta measured 8.4 cm. at the aortic valve, 10.2 cm. at a point 2 cm. above the valve, and 7.6 cm. at the arch of the aorta (Figs. 2 and 3). Marked left ventricular hypertrophy was present.

Lungs: The left lower lobe was atelectatic. The remainder of both lungs was nodular, crepitated poorly, and the cut surface exuded purulent material.

The liver, kidneys, and spleen were congested.

The brain and spinal cord were of normal weight and grossly were not remarkable.

The rest of the viscera were essentially normal.

Microscopic Examination.—Heart: There was a medial cystic necrosis in the aorta (Figs. 4 and 5), most severe in the aneurysmal part; however, it was found also in the carotid arteries and the abdominal aorta. The myocardium was hypertrophied. The vavular thickenings consisted of fibrous tissue.

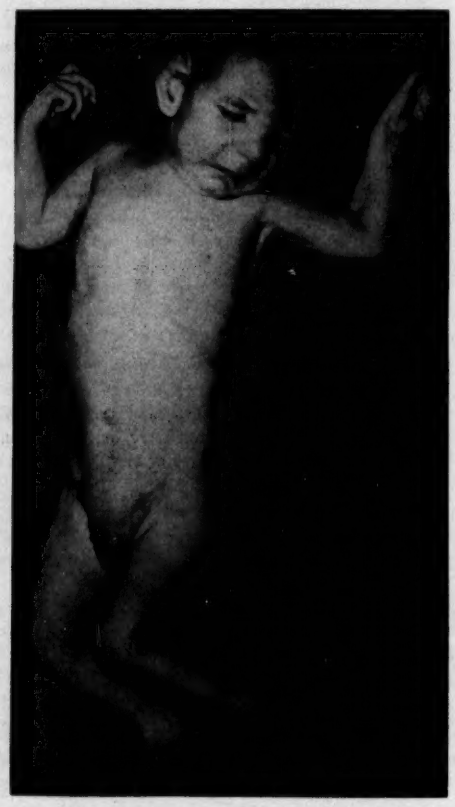

Fig. 1.—Infant in Case 1 showing arthrogryposis as well as the other features of Marfan's syndrome. Note the large ears.

Lungs: Severe bronchopneumonic changes were noted in all lobes except the left lower lobe, which was atelectatic.

Central Nervous System: The brain was unremarkable. The spinal cord, however, had a decrease in the number of anterior horn cells in its caudal part. This was determined by taking serial sections, counting the anterior horn cells, and averaging the number of cells in each section. The figure obtained was then compared to five control cases in which the same procedure was performed. The number of anterior horn cells was statistically diminished. However, very careful studies of the diaphragm, psoas, intercostal, gastrocnemius, and quadriceps muscles with phosphotungstic acid hematoxylin and eosin, and Mallory's aniline blue stains revealed no abnormalities of the skeletal muscles. The entire left knee joint was studied grossly and microscopically, and no abnormality was found.

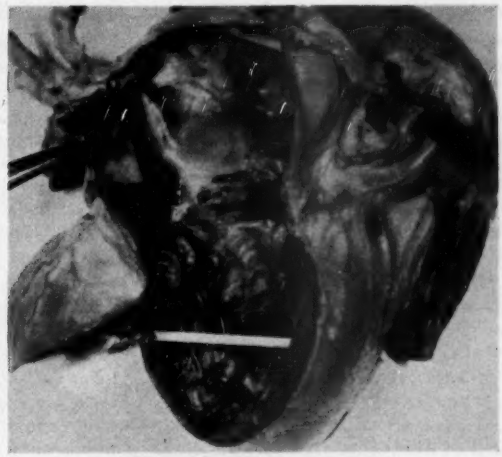

Fig. 2.—Gross heart in Case 1. Left atrium, mitral valve, and left ventricle. The atrium is enlarged and dilated. The peculiarly fenestrated and nodular mitral valve is visible. Left ventricular hypertrophy may be noted.

Fig. 3.—Gross heart in Case 1. Left ventricle and aorta. Left ventricular hypertrophy can again be seen. The aneurysm of the ascending aorta and the sinuses of Valsalva are recognizable.

There was no evidence of hydrocephalus, frontal atrophy, or pituitary disease in this case.

CASE 2 (Fig. 6).—H. S., a white boy was born Nov. 5, 1942. He was admitted to this hospital for the first time at one month of age. Three anomalies were present which were

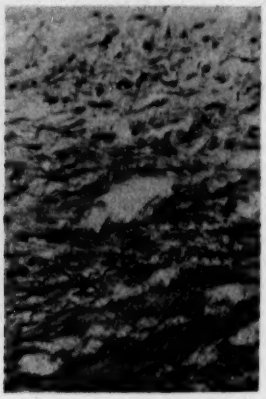

Fig. 4.—High-power photomicrograph showing the spaces of necrosis in the media with fragmentation of the elastic tissue (Case 1). Hematoxylin and eosin stain; × 250.

Fig. 5.—Low-power photomicrograph showing gross distortion of the architecture in the media of the aorta in Case 1. The cystic spaces are numerous. Hematoxylin and eosin stain; × 150.

responsible for many admissions to the hospital, namely, (1) cleft palate, (2) clubfeet, and (3) inguinal hernias. Hypertelorism and a small umbilical hernia were also discovered. At this time, the feet were put in casts, and he was referred to the outpatient department for further care.

Birth history revealed this boy to be the product of his mother's first pregnancy. Birth weight was 3,884 gm. (8 lb. 9 oz.). The labor was 24 hours long, and the mother had a placenta praevia. The neonatal period was normal. Family history was noncontributory.

During his lifetime this boy was admitted to our hospital as follows: His second admission was at 2 months of age for a bilateral inguinal herniorrhaphy, from which he made an uneventful recovery. At 7 months of age he was admitted for treatment of a severe upper respiratory infection. His fourth admission was at 10 months of age for repair of his cleft palate, which had failed to heal. When he was 2 years old, treatment was necessary for anemia. Another upper respiratory infection caused his sixth admission at 2⅓ years of age. When 2½ years of age, he had a re-repair of a left inguinal hernia, which was slow in healing. On his eighth admission, when 3 years of age, a basal systolic murmur and tachycardia were discovered for the first time. He had more reconstructive surgery for his cleft palate. At 4 years of age, his umbilical hernia was repaired, and his cleft palate was resutured. His cleft palate was again resutured at 5 years of age. This boy was a problem to the surgical staff because of his failure to heal well following his operations. Orthopedic surgery for his clubfeet accounted for his 11th and 12th admissions at 6 and 6½ years of age, respectively. At this time, a prominence of his lower sternum was noted. When he was 7 years of age, his palate was again repaired. There were subsequent admissions in 1950 (8 years of age) for a tonsillectomy and further cleft palate plastic surgery. In addition to admissions to the hospital, he was seen frequently in the outpatient department for arachnodactyly, treatment of respiratory infections, and atopic eczema. In 1948, at 5 years 3 months of age, the characteristics of arachnodactyly were described for the first time. His heart murmur, which was noted at 3 years of age, had not been audible to other examiners over the course of years.

His contagion history was as follows: measles at 14 months of age, scarlet fever at 5 years, chickenpox at 7 years, and pertussis at 8 years of age.

In July, 1952, he was readmitted for study because a heart murmur had been discovered at school upon routine examination. There were absolutely no symptoms referable to the heart. Positive physical findings were as follows: The patient was thin, with a prominent lower sternum and Harrison's groove. The extremities were long and thin with tapering phalanges, characteristic of arachnodactyly. The cardiac apex beat was in the sixth left interspace, just medial to the nipple line. There was a Grade-II systolic murmur heard over the precordium, best heard at the apex. Also at the apex there was a crescendo diastolic murmur ending with the first heart sound. A diastolic murmur beginning with the second sound was also heard best to the right of the sternum in the second to fourth interspaces. A thrill was palpable along the right sternal margin. A faint femoral thud was heard. The spleen was not palpated. The liver was at the costal margin. A capillary pulse was not obtained. Blood pressure was 110/60 mm. of Hg.

An amazing dilatation of the aortic arch was seen at fluoroscopy and on the chest roentgenograms. Left axis shift with first-degree A-V block was seen on electrocardiogram.

As there were no symptoms, the boy was discharged without treatment and was to be followed in the outpatient department.

His 20th, the final, hospital admission was Dec. 30, 1952. He had a five-day history of intermittent vomiting associated with an upper respiratory infection, a cough for two and a half weeks, and fatigue and arm and leg pain for a period of "several weeks." On the morning of Nov. 29, while out shopping with his mother, he suddenly began to complain of severe pain in the right chest, and he felt extremely tired. He was put to bed and digitalized by the family physician. The pain subsided that evening. However, the fatigue persisted. A pallor was also noticed at this time. His exercise tolerance had markedly diminished, and his condition had generally deteriorated.

Physical examination revealed an ill-appearing, thin, pale, and mildly dyspneic child. He weighed 25.4 kg. (56 lb.) and measured 136 cm. (53½ in.). His head was dolichocephalic, with large soft flapping ears. There was hypertelorism, but no evidence of lens pathology. This was confirmed by ophthalmological consultation. There was no evidence of ear, nose, or throat infection. He had a prominent lower sternum. The extremities were long and thin, with tapering phalanges. There was edema of the shins. Healed herniorrhaphy scars were evident. The cardiac apex was in the sixth left interspace at the nipple line. A Grade-II

systolic murmur together with a presystolic murmur were best heard near the apex. Along the right sternal border a soft blowing diastolic murmur was heard, beginning with the second sound. Posteriorly, there was dulness over the base of the right lung with distant breath sounds and medium moist rales. Above this area was bronchial breathing. Femoral thuds were

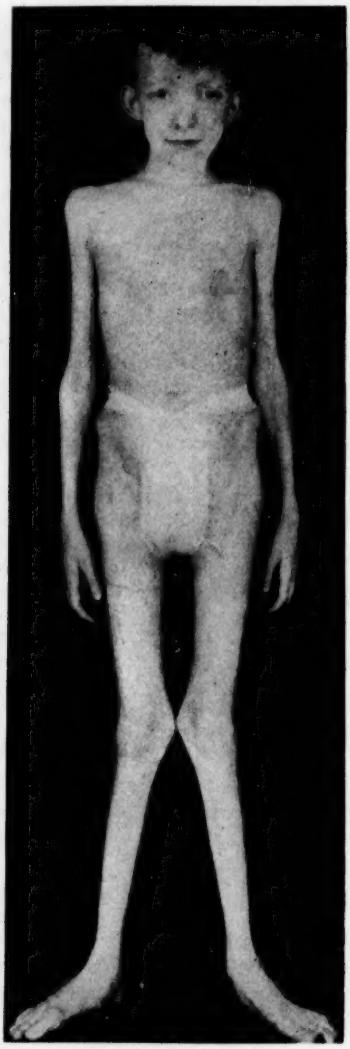

Fig. 6.—Patient in Case 2 revealing gross characteristics of Marfan's syndrome.

present. The spleen was not palpated. The liver was palpated 3 cm. below the right costal margin. The blood pressure was 114/60 mm. of Hg in each arm, and 135/60 in each leg. Pulse was 112 per minute; respirations were 36 per minute.

Laboratory data were as follows: Hemoglobin, 13 gm. per 100 cc.; RBC 4,640,000; WBC 10,100, with a normal differential count. Results of Mantoux and serology tests were negative.

Urinalysis was free of albumin, glucose, and microscopic elements. Tremendous cardiac and aortic enlargement was seen on the chest roentgenogram. The findings on electrocardiogram were essentially as in July, 1952.

He was afebrile throughout his hospital course.

The boy was digitalized, placed in oxygen, and given diuretics and penicillin. However, he gradually became worse in spite of this treatment, and died Jan. 21, 1953.

Pathological Summary.—The autopsy was performed 12 hours after death. The body measured 136 cm. in length. The external appearance was as described in the physical examination. Through a primary Y-shaped incision, the chest and the abdomen were explored. There was a paucity of subcutaneous fat. The findings of most interest were limited to the cardiovascular system. When the chest was opened, the lungs were obscured by an enlarged heart which filled the entire anterior chest. The pericardial cavity contained 60 cc. of light straw-colored fluid. The heart weighed 900 gm. (normal 116 gm.), and all chambers were dilated and hypertrophied. The most marked hypertrophy was left ventricular, the musculature measuring 1.5 cm. in its greatest thickness. The tricuspid valve measured 12 cm. in circumference, the mitral valve 9 cm., the pulmonary valve 6.8 cm., and the aortic valve 12 cm. Distal to the aortic valve was a fusiform aneurysm of the entire ascending aorta. This aneurysm measured 14 cm. in its greatest diameter, and grossly had three large tears, passing through intima and media. A thin layer of adventitia covering the outer layer of the tears prevented rupture. The largest defect measured 4 cm. by 1 cm. and was situated on the posterior wall of the aorta, 6 cm. above the aortic valve. Another lesion was on the anterolateral aortic wall in the same region and measured 3.6 cm. by 0.8 cm. in size. The third tear was 2 cm. by 0.4 cm. and was located just above the sinus of Valsalva on the posterior aortic wall. The aortic valve cusps were thickened, and the coronary ostia arose high in the sinus of Valsalva. No thickening or other abnormality of the tricuspid or mitral valves was noted.

All organs revealed severe passive congestion. There was a large triangular area of pulmonary infarction in the right lower lobe of the lung which appeared to be of recent origin. The left lower lobe was atelectatic. The brain was grossly unremarkable.

Microscopic Examination.—Heart: Medial cystic necrosis was present in all sections of aorta examined, but was most severe in the region of the aneurysm (similar findings in Case 1, Figs. 4 and 5). The aortic valvular thickening was composed mainly of fibrous tissue. Hypertrophy of the muscle fibers in the left ventricle was severe.

Lungs: The gross impression of pulmonary infarction was substantiated by microscopic examination. Chronic passive congestion and left lower lobe atelectasis were also noted.

Liver, kidneys, and spleen: These organs revealed severe chronic passive congestion. No abnormalities of the spinal cord, brain, or skeletal muscles could be found.

COMMENT

Arachnodactyly is a congenital syndrome characterized by "spider hands and feet," muscular atrophy, and often ocular and cardiac anomalies. This syndrome was first described by Marfan, in 1896. There have been numerous case reports and descriptions in the literature, a few of which are noted in the bibliography.†

Numerous theories have been presented as to the cause of this condition. One thought is that this is a form of muscular dystrophy closely related to amyotonia congenita. This is evidenced by the fibrillating tongue, muscular atrophy, and arthrogryposis. However, though there is nothing definite concerning its origin, Marfan's syndrome appears more closely related to amyotonia congenita than to any other condition.

Normally, a patient with Marfan's syndrome has weak musculature, and deep reflexes are present. Arthrogryposis has been noted to be associated with Marfan's syndrome.

† References 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, and 21.

Another thought is that it is an endocrine disorder. The most accepted theory is that this condition is caused by a defect in the mesodermal cells of the embryo. About 30% of the cases are hereditary and familial.

The most striking feature of this syndrome is the increase in length of the bones of the hands and feet, particularly the metacarpal, metatarsal, and phalangeal bones. These bones usually show rarefaction, especially at the metaphysis.

Abnormality of the skull occurs in 80% of all cases. The skull is usually dolichocephalic. Prominent supraorbital ridges, frontal bosses, and prognathism are common. The anterior fontanel is usually patent. There is poor development of the inferior maxilla. The teeth are usually normal, and the palate is narrow and highly arched.

There is marked atrophy of the entire musculature, particularly the muscles of the extremities. Laxity of the joints with abnormal motility is common. Contractures of the fingers and toes occur. The patient may have webbing of the fingers. The lips are thin. There is an absence or decrease in subcutaneous fat. The chest wall is thin.

The external ears are enlarged, having a deficiency of cartilage and an overdeveloped helix.

Bilateral eye abnormalities occur in over 50% of the cases. Luxation or subluxation of the lens occurs most frequently. Almost all cases are bilateral. Also seen are congenital hydrophthalmus, small pupils and iridodesis, strabismus, transient nystagmus, and marked myopia.

Congenital heart disease is seen in approximately 90% of autopsied cases.

Affected children are taller, but weigh less than normal children of the same age. The basal metabolic rate and blood pressure are low. The results of blood chemistry and urinary tests are normal. Mentality is usually reported as being normal. However, mental retardation is not uncommon and has been seen by us in other patients with this condition.

There is no cure for this syndrome, but there may be an improvement of signs with orthopedic and ophthalmological aid. These persons lead a moderately sheltered existence, as physical exercise is contraindicated. Few attain old age, as they are subject to frequent respiratory infections, especially pneumonia. The majority die before reaching maturity.

In discussing the two cases presented in this article, few findings are noted which give any clue as to the cause and pathogenesis of this disease. The presence of medial aortic necrosis in a 9-month-old infant tends to substantiate the opinion of most authors that this disease is hereditary and is not an acquired weakness. Unfortunately, we were unable to dissect or outline the vasavasorum in either case; however, numerous microscopic sections of the aorta failed to reveal any abnormalities in these structures.

The incidence of the disease is undoubtedly much higher than the literature would lead one to believe. From a collection of 356 congenital malformations of the heart at the Children's Memorial Hospital, two specimens are from patients with arachnodactyly who had died with aortic aneurysms—an incidence of about 0.7%. However, this does not reflect the true incidence, as most of these patients die beyond the pediatric age limit. There is at the present time in the outpatient clinics of the Children's Memorial Hospital a one-year-old infant with arachnodactyly

whose mother and grandmother died in early adult life. They were autopsied at a general hospital. In both instances the autopsy findings revealed a dissecting aortic aneurysm.

On reviewing the literature pertaining to the cardiac disease in Marfan's syndrome, one immediately notes the frequency of rheumatic heart disease in the living patients and its rarity in autopsied specimens.

From the 21 autopsied specimens of arachnodactyly, only two revealed any evidence of rheumatic heart disease. One patient had subacute bacterial endocarditis. From the remaining 18 hearts, nine specimens revealed a deformed mitral or tricuspid valve. The authors in these articles, although describing the deformities, failed to give a diagnosis of their origins. In our first case, grossly deformed mitral and tricuspid valve were noted, which were probably congenital in origin, but certainly not rheumatic in origin. From the pathology present one can easily deduce how murmurs closely resembling those of rheumatic heart disease could be present. One should, therefore, be very cautious in making a diagnosis of rheumatic heart disease in these patients unless substantiated by typical clinical and laboratory findings.

It is of interest to note that, despite a diligent search, no histological abnormality was discovered in the endocrine, musculoskeletal, or central nervous systems.

SUMMARY

Two cases exemplifying the typical findings of Marfan's syndrome with an associated aortic aneurysm have been presented. These are the 20th and 21st autopsied cases to appear in the literature. We believe these two patients (9 months and 10 years of age, respectively) to be the youngest possessing arachnodactyly and aortic aneurysm in reported cases. To our knowledge, this 9-month-old boy is the first infant to have died of this disease.

Dr. Stanley Gibson gave permission for the use of these two cases of his patients and also gave advice and assistance in the preparation of this article.

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FETAL AND ADULT HEMOGLOBINS IN HEMOLYTIC DISEASE OF THE NEWBORN

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IT HAS long been known that the period of fetal life is characterized by the synthesis of a distinct type of hemoglobin which is gradually, and finally completely, replaced by another type which is found in the blood of older infants, children, and adults. Differences between fetal and adult hemoglobin were first shown by von Korber [1] in 1866 and von Krüger [2] in 1887, both of whom demonstrated an increased resistance to alkali denaturation of the hemoglobin derived from fetal red cells. Many subsequent investigations have confirmed these observations, not only in humans, but also in many of the animal species as well.* In addition to differences in response to alkali denaturation, the two types of hemoglobin have been found to differ in oxygen and carbon dioxide affinity,† chemical structure,[13] immunological properties ‡ crystalline configuration,[16] and electrophoretic mobility.§ Most investigators have indicated that the differences lie in the globin portion of the molecule, the heme apparently being identical in the two types of pigment.[19]

Early studies indicated that adult hemoglobin began to be formed at some point during the third trimester of intrauterine life and that the fetal pigment disappeared completely by 4 to 7 months after birth.|| Recent investigation by Singer, Chernoff, and co-workers have added greatly to the knowledge of fetal hemoglobin and have led to modification of the method of alkali denaturation so that minute quantities of fetal pigment can be detected with great accuracy. These workers have studied the concentration of fetal hemoglobin in the blood of infants and children and have demonstrated that significant amounts may persist up to 30 months of age and, in some rare persons, even up to 4 years of age.[23] Of great interest, too, has been the finding by Singer and Chernoff [20] of large quantities of fetal hemoglobin in the

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* References 3, 4, 5, 6, 7, 8, 9, and 10.

† References 11 and 12.

‡ References 14 and 15.

§ References 17 and 18.

|| References 4 and 5.

blood of children and adults with various hematological disorders, particularly sickle-cell and Mediterranean anemias. The full significance of these interesting findings remains to be elucidated.

In the study of the physiology and pathology of blood formation in the fetus and infant, further knowledge of the properties, behavior, and significance of the fetal hemoglobin seems of basic importance, for here one deals with a mechanism which serves as a foundation for the later development of normal hematopoiesis. It seems logical that disorders of the blood which are manifest in the prenatal, neonatal, or infancy period might be understood more completely through investigation of the quantitative relationships between fetal and adult hemoglobins.

In hemolytic disease of the newborn, the hematopoietic system of the fetus and newborn infant is subjected to a severe and sometimes overwhelming stress. For variable periods of time during intrauterine life and with varying degrees of efficiency, the fetal hematopoietic organs are called upon to replace red cells and hemoglobin which are destroyed by hemolysis. The significance of fetal hemoglobin in hemolytic disease of the newborn has come under study by several workers, but the conclusions drawn from these investigations differ greatly.

In 1948 Jonxis ¶ claimed to have found large amounts of adult hemoglobin in the blood of infants affected with hemolytic disease of the newborn. In addition, he stated that only cells containing fetal hemoglobin were destroyed in the hemolytic process. In 1943, however, Mollison,[27] by transfusing Rh-positive adult blood into infants with hemolytic disease, had demonstrated that there was indiscriminate destruction of the babies' and donors' cells, thus indicating that the hemolysis was dependent upon the antigenic structure of the red cell, rather than upon its content of hemoglobin. Baar [28] also denied Jonxis' hypothesis of selective destruction of fetal hemoglobin-containing cells and demonstrated that fetal hemoglobin could be synthesized postnatally in the face of severe hemolytic disease of the newborn. In 1949, Ponder and Levine [29] determined the concentrations of fetal hemoglobin in the cord blood of a group of infants with hemolytic disease and could find no difference from a control group of normal infants. In this series, however, the determinations of fetal hemoglobin in 22 diseased and 22 normal infants were carried out by alkali denaturation at pH of 11.7, a method which has been shown to yield inaccurate results.[20] In only seven diseased infants and seven controls were the determinations carried out at pH 12.7, the presently accepted technique for most accurate results. Because of the divergent opinions and because of the small number of cases in all reported studies, it was considered advisable to reinvestigate the problem.

MATERIALS AND METHODS

Fetal hemoglobin concentrations were determined on the cord-blood specimens obtained from 96 normal full-term infants and from 33 consecutively born infants with hemolytic disease. The cord blood was taken at the time of delivery and was collected in bottles containing dried heparin. On the same samples of blood the total hemoglobin concentration was determined photoelectrically in the Evelyn colorimeter.

All infants in the group with hemolytic disease had positive results on Coombs's tests, and all mothers of these babies gave serological evidence of Rh sensitization. Of the 33 infants, 21 were treated by exchange transfusions, while 12 received small transfusions or required no

¶ References 25 and 26.

therapy at all. In patients who received replacement transfusions, cord samples were also taken for analysis at the beginning and at the end of the procedure. Subsequent determinations of fetal hemoglobin concentrations were made on samples of capillary or venous blood.

Fetal hemoglobin concentrations were determined exactly as described by Singer and Chernoff.[20] In this method an approximate 10% hemoglobin solution is denatured for exactly one minute by N/12 NaOH (pH 12.7), the reaction being halted and the denatured hemoglobin precipitated by addition of an ammonium sulfate reagent. The hemoglobin concentration in

TABLE 1.—*Fetal and Adult Hemoglobin Concentrations in Cord Blood of Normal Newborn Infants*

Measurement in Cord Blood	Mean ± S. D.	Standard Error of Mean
Fetal hemoglobin, %.....	71.0 ± 7.7	0.790
Fetal hemoglobin, gm./100 cc.....	11.6 ± 1.8	0.207
Adult hemoglobin, gm./100 cc.....	4.7 ± 1.3	0.149
Total hemoglobin, gm./100 cc.....	16.4 ± 1.1	0.126

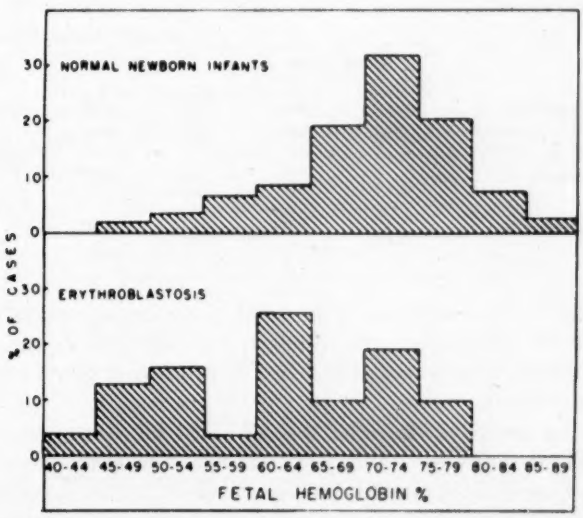

Fig. 1.—Distribution of the values for percentage of fetal hemoglobin in the cord bloods of normal infants and infants with hemolytic disease. It may be seen that the normal curve is skewed to the left in the group of infants with hemolytic disease of the newborn.

the filtrate (undenatured) is determined photoelectrically, and the percentage of undenatured hemoglobin (fetal hemoglobin) is calculated. Recent immunological studies by Chernoff [15] have demonstrated that the undenatured pigment is indeed fetal hemoglobin.

RESULTS

1. Normal Controls.—Table 1 lists the values for the percentage of fetal hemoglobin and for the concentrations (in grams per 100 cc.) of total, fetal, and adult hemoglobin in the cord blood of 96 normal full-term infants.

II. Erythroblastotic Infants.—If, as Jonxis [25] has stated, fetal-hemoglobin-containing cells were preferentially destroyed, one would expect in hemolytic disease (*a*) that the percentage of fetal hemoglobin at birth would be significantly lower in infants with hemolytic disease than in normal newborns, (*b*) that the percentage of fetal hemoglobin would correlate with the degree of anemia, i. e., that those infants demonstrating the lowest percentage of fetal hemoglobin would likewise demonstrate the greatest degree of anemia; in addition it would be anticipated that the percentage of fetal hemoglobin would correlate with the quantity of fetal hemoglobin in grams per 100 cc., i. e., that lowering of the per cent fetal hemoglobin would be represented by an actual loss of fetal hemoglobin, (*c*) that the percentage of adult hemoglobin would have no correlation with the quantity of adult hemoglobin, i. e., the absolute quantity of adult hemoglobin would remain unchanged as the relative amount varied by virtue of selective change in fetal hemoglobin. As a corollary of this, one would expect no relationship between the quantity of adult hemoglobin and the level of anemia.

TABLE 2.—*Comparison of Fetal and Adult Hemoglobin Concentrations in Normal Infants and Infants with Hemolytic Disease*

	Normal Infants		Hemolytic Disease, Entire Group		
Measurement	Mean ± S. D.	S. E. of Mean	Mean ± S. D.	S. E. of Mean	Significance of Difference of Mean from Normal
Fetal Hb., %.....	71.0 ± 7.7	0.790	62.8 ± 9.9	1.73	$t = 4.91$ $P = <0.01$ Highly signif.
Fetal Hb., gm./100 cc.....	11.6 ± 1.18	0.207	8.4 ± 2.5	0.435	$t = 2.40$ $P = <0.05 >0.01$ Prob. signif.
Adult Hb., gm./100 cc.....	4.7 ± 1.3	0.149	5.1 ± 1.8	0.303	$t = 1.75$ $P = >0.05$ Not signif.

Chart 1 depicts the distribution of the values for percentage of fetal hemoglobin at birth in the 96 normal and in the 33 infants with hemolytic disease. It may be seen that the normal curve is skewed to the left in the group of babies with hemolytic disease of the newborn.

Table 2 lists the mean values for the per cent fetal hemoglobin and for the concentrations (in grams per 100 cc.) of total, fetal, and adult hemoglobin in the entire group of infants with hemolytic disease and the statistical comparison of these values with those of the control group. As may be seen, the percentage of fetal hemoglobin in the entire group of infants with hemolytic disease (62.8 ± 9.9) was found to be significantly lower than normal (P is <0.01). The quantity of fetal hemoglobin (in grams per 100 cc.) in the blood of infants with hemolytic disease (8.4 ± 2.5) was probably significantly lower than normal (P is $<0.05 >0.01$). On the other hand, the quantity of adult hemoglobin (5.1 ± 1.8) was not significantly different from the normal (P is >0.05).

The above results would seem to be in agreement with Jonxis' hypothesis in that the per cent fetal hemoglobin and the grams per 100 cc. fetal hemoglobin are below normal, while the level of adult hemoglobin (grams per 100 cc.) is no different from normal.

Chart 2, however, demonstrates the relationship between the per cent fetal hemoglobin at birth and the total hemoglobin concentration, and it may be seen that no correlation exists between the per cent fetal hemoglobin and the degree of anemia. Thus low percentages of fetal hemoglobin are found with equal frequency in infants who are severely anemic and in those who are nonanemic. This finding, then, is in direct contradiction to Jonxis' hypothesis, since, as pointed out earlier, a preferential destruction of fetal hemoglobin would lead to a correlation between per cent fetal hemoglobin and the degree of anemia.

Chart 3 demonstrates the relationship between each type of hemoglobin and the total hemoglobin concentration in the cord blood of the group of infants with hemolytic disease. It may be seen that both the fetal and the adult hemoglobin values

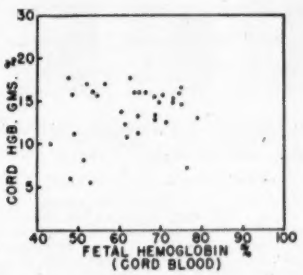

Fig. 2.—The relationship between the percentage of fetal hemoglobin and the total hemoglobin concentration in the cord blood of infants with hemolytic disease of the newborn. The lack of correlation denies the hypothesis that preferential destruction of fetal-hemoglobin-containing red cells occurs.

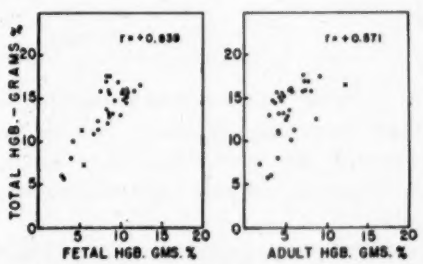

Fig. 3.—The relationship between the concentrations of fetal and adult hemoglobin and the total hemoglobin concentration in the cord blood of infants with hemolytic disease of the newborn. The good correlation between the concentration of each type of hemoglobin and the total hemoglobin concentration indicates that loss of both types is involved in the hemolytic process.

correlate with the total hemoglobin concentration, low levels of each tending to be associated with anemia and high levels of each with normal hemoglobin levels at birth. Thus, here, as in Chart 2, the data deny Jonxis' [25] claim of preferential destruction of fetal hemoglobin and indicate that loss of both types of hemoglobin is involved in the hemolytic process of hemolytic disease of the newborn.

It becomes evident, therefore, that the apparent contradiction between the lowered percentage of fetal hemoglobin in hemolytic disease and the lack of evidence for selective destruction of fetal hemoglobin cannot be resolved by considering the forces of destruction alone; the factor of hemoglobin regeneration in the presence

of the disease process must also be taken into account. Thus, an abnormally low percentage of fetal hemoglobin might occur if there were preferential regeneration of adult hemoglobin rather than preferential destruction of fetal hemoglobin.

As was demonstrated above (Table 2) the quantity of fetal hemoglobin in infants with hemolytic disease was significantly lower than normal, while the quantity of adult hemoglobin was not significantly different from normal. If preferential regeneration of adult hemoglobin occurred in hemolytic disease of the newborn, one might expect that infants born with normal hemoglobin levels would demonstrate quantities of adult hemoglobin greater than normal, i. e., that adult hemoglobin regeneration would serve as a compensatory reaction to the hemolytic process. In order to investigate this possibility, the series of cases of infants with hemolytic disease was divided into two groups, anemic and nonanemic, based on the level of cord hemoglobin at birth. As was demonstrated earlier, the mean cord-hemoglobin level of normal infants was found to be 16.4 ± 1.1 gm. per 100 cc. A cord-hemoglobin level

TABLE 3.—*Fetal and Adult Hemoglobin Concentrations in Normal Infants, Anemic Infants with Hemolytic Disease, and Nonanemic Infants with Hemolytic Disease*

	Normal Infants		Hemolytic Disease, Cord Hb.<14.2 Gm./100 Cc.			Hemolytic Disease, Cord Hb.>14.2 Gm./100 Cc.		
Measurement	Mean ± S. D.	S. E. of Mean	Mean ± S. D.	S. E. of Mean	Significance of Diff. of mean from Normal	Mean ± S. D.	S. E. of Mean	Significance of Diff. of Mean from Normal
Fetal Hb., %.....	71.0 ± 7.7	0.790	62.5 ± 9.5	2.40	$t = 3.88$ $P < 0.01$ Highly signif.	63.4 ± 9.7	2.37	$t = 3.53$ $P < 0.01$ Highly signif.
Fetal Hb., gm./100 cc.....	11.6 ± 1.8	0.207	6.8 ± 2.4	0.60	$t = 7.09$ $P < 0.01$ Highly signif.	9.9 ±1.4	0.339	$t = 3.58$ $P < 0.01$ Highly signif.
Adult Hb., gm./100 cc.....	4.7 ± 1.3	0.149	4.1 ± 1.2	0.30	$t = 0.65$ $P > 0.1$ Not signif.	5.9 ± 1.6	0.387	$t = 3.39$ $P < 0.01$ Highly signif.

of 14.2 gm. per 100 cc. or below (mean normal-hemoglobin minus 2 S. D.) was therefore taken to indicate the presence of anemia. On the basis of this division 16 of the infants with hemolytic disease were found to be anemic and 17 nonanemic at birth. The results in each group and their statistical comparison with the normal are demonstrated in Table 3.

In both the anemic and nonanemic groups the per cent fetal hemoglobin at birth and the quantity of fetal hemoglobin (grams per 100 cc.) were found to be significantly lower than normal (P is <0.01). The quantity of adult hemoglobin in the two groups, however, differed. In the anemic group the quantity of adult hemoglobin was not significantly different (higher or lower) than normal (P is >0.1); in the nonanemic group, however, the amount of adult hemoglobin present in the cord blood at birth was significantly higher than normal (5.9 ± 1.6 versus 4.7 ± 1.3; P is <0.01). The results are shown graphically in Chart 4.

The above findings appear to indicate that the regeneration of adult hemoglobin is one of the mechanisms serving to protect the infant against the hemolytic anemia. This regeneration, however, cannot be the sole reason for the maintenance of a high hemoglobin level in some infants with hemolytic disease, since scrutiny of the data reveals that in these babies the entire hemolytic process is of less severity. This

conclusion is indicated by the fact that in this group of infants the level of fetal hemoglobin, while lower than normal, is much higher than that found in infants born anemic.

That the regeneration of adult hemoglobin is indeed selective may also be seen from the data in the anemic group. Here, where evidence of a severe hemolytic

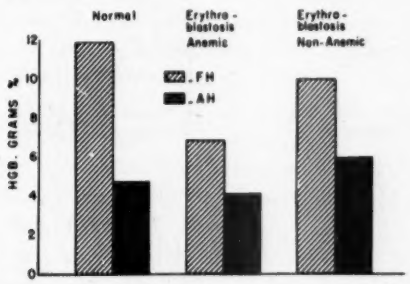

Fig. 4.—Graphic representation of the fetal and adult hemoglobin concentrations in normal infants, anemic infants with hemolytic disease, and nonanemic infants with hemolytic disease (Table 3).

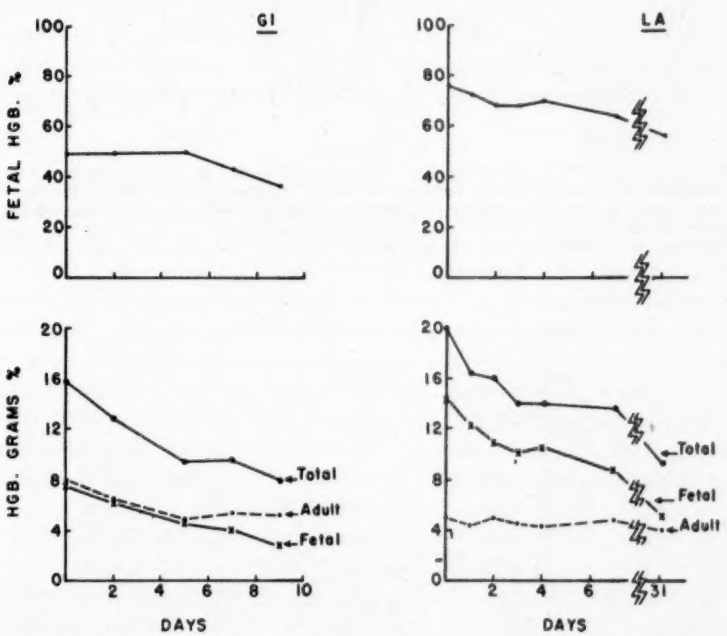

Fig. 5.—Changes in the percentage of fetal hemoglobin and in the concentrations of fetal, adult and total hemoglobin in two infants with mild hemolytic disease of the newborn who received no therapy. In infant Gi. (left) there occurs a steady fall in both fetal and adult hemoglobin levels for five days, following which the adult hemoglobin level remains steady as the fetal hemoglobin continues to fall. In infant La. (right) the adult hemoglobin concentration remains level from birth as the fetal hemoglobin falls steadily.

process is indicated by the very low levels of fetal hemoglobin, the adult hemoglobin concentration is still maintained at levels found in normal infants.

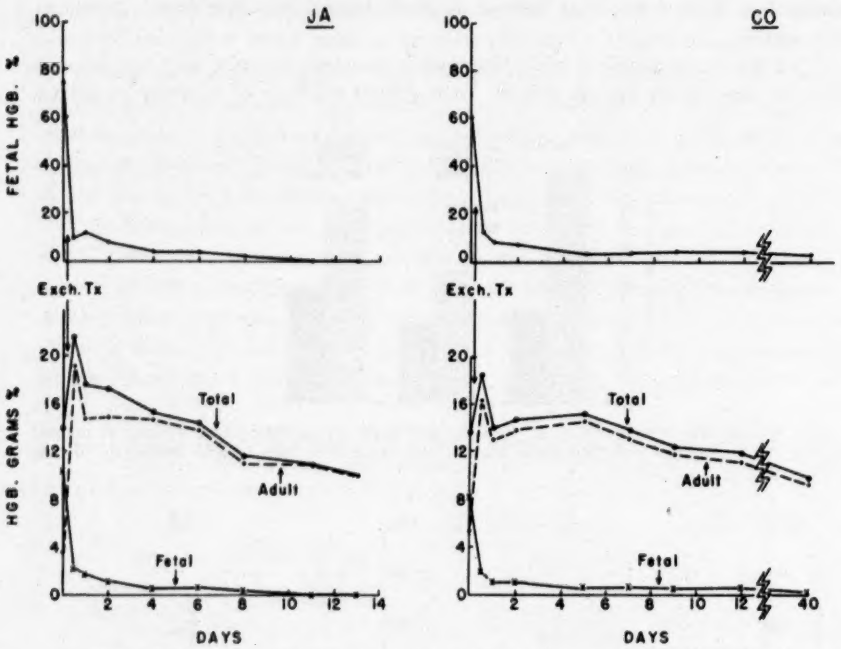

Fig. 6.—Changes in the percentage of fetal hemoglobin and in the concentrations of fetal, adult and total hemoglobin in two infants with severe hemolytic disease of the newborn who were treated by exchange transfusion. In Ja. (left) the fetal hemoglobin disappears completely in 11 days following exchange transfusion. In Co. (right) significant amounts of fetal hemoglobin are still present 40 days following replacement transfusion.

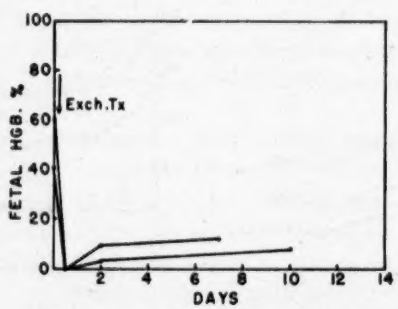

Fig. 7.—Demonstration of the postnatal production of fetal hemoglobin. In the two infants above complete removal of fetal hemoglobin by exchange transfusion is followed by return of significant amounts of the pigment in subsequent days.

The above data were derived from analyses on cord blood at the moment of birth and represent changes which have occurred during prenatal life. The changes in fetal and adult hemoglobins after birth were of several types and seemed to depend upon severity of disease and upon individual capacity for hemoglobin regeneration. In some infants, with mild hemolytic disease, the fetal hemoglobin fell gradually while the adult hemoglobin remained at a steady level from birth. In other babies, both types of hemoglobin fell concomitantly for several days and then, as the fetal hemoglobin continued to fall, the adult hemoglobin assumed a plateau. Examples of these two types of reactions are shown in Chart 5.

In cases where exchange transfusion was performed, individual differences in the postnatal fate of the fetal hemoglobin were noted. In some infants, the fetal hemoglobin fell steadily after replacement transfusion and disappeared completely in two weeks. In others, however, appreciable amounts of fetal hemoglobin were still present after a month (Chart 6).

In several infants in whom exchange transfusions were performed, it was possible to demonstrate that some production of fetal hemoglobin also occurs postnatally. Thus, in two infants in whom fetal hemoglobin was completely removed by exchange transfusion, a significant amount of the pigment was found to have returned in subsequent days (Chart 7). These findings are similar to those reported by Baar.[28] Parenthetically, it may be noted that the determination of fetal hemoglobin concentrations immediately before and after replacement transfusion may serve as an index of efficiency of exchange.

COMMENT

These findings in the present study are in partial agreement with those of Jonxis [25] in that greater than normal quantities of adult hemoglobin have been found at birth in the blood of infants with hemolytic disease. There appears to be no evidence, however, that fetal hemoglobin is preferentially destroyed in hemolytic disease of the newborn or, as claimed by Jonxis, that the antibodies behave differently on cells containing fetal hemoglobin than on cells containing adult hemoglobin. From a teleological viewpoint, it would seem strange that preferential regeneration of adult hemoglobin takes place at a time when fetal hemoglobin usually constitutes over two-thirds of the fetus' total hemoglobin content. The demonstration by Singer and Chernoff [20] that in congenital hemolytic syndromes there is either a persistence or renewal of fetal hemoglobin production in older children and adults makes this preference for adult hemoglobin in the fetus even more perplexing. Since it is known that adult hemoglobin begins to appear at least by the third trimester of gestation, it might be suggested that the type of hemoglobin synthesis constitutes the only one available at that time and that the fetal hemoglobin in the circulating blood represents that which is formed much earlier and which, upon destruction, is not replaced. However, studies in our laboratory have revealed that in normal circumstances large amounts of fetal hemoglobin are synthesized during the last trimester of gestation.[30] In addition, it has been demonstrated by Baar [28] and in the present study that fetal hemoglobin may be produced postnatally. It might also be suggested that fetal and adult hemoglobins are synthesized in different areas and that the excessive extramedullary hematopoiesis characteristic of hemolytic disease of the newborn might explain the predominance of adult hemoglobin. Embryologically,

however, hepatic hematopoiesis is predominant at a stage in development when fetal hemoglobin is, apparently, the sole type of hemoglobin manufactured. In addition, Jonxis [26] was unable to detect any difference in fetal hemoglobin in blood derived from bone marrow and that derived from liver. Likewise, we have found in several determinations that the percentages of fetal hemoglobin in marrow and venous blood are identical. It appears, therefore, that synthesis of either type of hemoglobin is not determined by anatomical site of hematopoiesis, but rather by a strongly entrenched developmental pattern in the fetus. Additional evidence that the young infant depends primarily upon synthesis of adult hemoglobin in response to demand was presented by Adams,[31] who demonstrated that in infants with cyanotic congenital heart disease and polycythemia the fetal hemoglobin levels were no different from those in normal infants of comparable age. These findings have been confirmed in our own laboratory. Here too, it might have been anticipated on teleological grounds that an infant requiring large quantities of additional hemoglobin in response to anoxia would have exhibited a persistence of fetal hemoglobin synthesis.

The present studies have indicated that some degree of excessive intrauterine hemolysis probably occurs even in those infants with hemolytic disease who were born with normal hemoglobin levels and without demonstrable clinical evidence of disease at birth. This may be deduced from the fact that the fetal hemoglobin concentrations in these babies are almost invariably below normal, and it appears that the capacity to synthesize adult hemoglobin serves to maintain the total hemoglobin concentration at normal levels in these infants.

SUMMARY AND CONCLUSIONS

Fetal and adult hemoglobin levels were determined in the cord bloods of 96 normal infants and 33 infants with hemolytic disease.

The percentage of fetal hemoglobin was significantly lower in the group of infants with hemolytic disease than in the control group.

In the entire group of infants with hemolytic disease, the concentration (in grams per 100 cc.) of fetal hemoglobin was found to be significantly lower than normal, while the concentration of adult hemoglobin was found to be no different from that in normal infants.

When the group of infants with hemolytic disease was divided on the basis of the degree of anemia present at birth, it was found that those infants born with normal hemoglobin levels demonstrated concentrations of adult hemoglobin which were greater than normal.

No evidence could be elicited to indicate that preferential destruction of fetal-hemoglobin-containing erythrocytes takes place in hemolytic disease of the newborn. On the other hand, preferential regeneration of adult hemoglobin in response to hemolysis does appear to be significant in this disease.

The degree of anemia manifested at birth by an infant with hemolytic disease of the newborn seems to depend both upon the severity of the hemolytic process and upon the individual capacity for hemoglobin regeneration. In those infants born with normal hemoglobin levels, the capacity to synthesize adult hemoglobin in amounts greater than normal appears to be an important mechanism serving to prevent anemia.

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NEUROGENIC STRIDOR IN INFANCY

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THE SYMPTOMS of inspiratory laryngeal stridor, as frequently seen in pediatrics, fall into a wide spectrum of diseases that constitute a perplexing problem of differential diagnosis. At one end of the scale are found those infants who have nothing more than inspiratory stridor which interferes with the usual feeding techniques; the mothers are frequently reassured, without detailed diagnostic studies, that this is due to a minor epiglottic abnormality which, in the course of the first year of life, will correct itself and is commonly called "congenital laryngeal stridor." [1]

The other end of the spectrum is less well defined and includes those infants with symptoms of laryngeal stridor in association with apnea and cyanosis. Such infants are frequently thought to represent a "convulsive disorder" or "feeding problem" or may even be treated for the now generally unacceptable condition of an "enlarged thymus." Detailed clinical studies often demonstrate a normal child or one with some abnormality seemingly not related to the primary difficulty.

We were immediately concerned with a problem such as this in the two infants to be discussed in detail in this paper; two other babies survived our ignorance and in retrospect should be included in this group. In the light of our experience with these infants, we now believe that symptoms of stridor, apnea, and cyanosis can be precipitated by a neurogenic mechanism differing from "idiopathic convulsions" by the presence of a "trigger mechanism" which is identifiable and capable of reproducing attacks when stimulated. Even more important, however, is the recognition of this mechanism which permits the successful direction of therapy toward depression of the "trigger" or the end organs stimulated by its activity.

Our first patient (Case 1) was seen in the University Hospital at the age of 2 months because of intermittent attacks of stridor, apnea, cyanosis, and unconsciousness. There followed seven months of hospitalization during which four laryngoscopies, two bronchoscopies, one esophagoscopy, and a tracheogram did not establish a diagnosis. Finally, a thoracotomy with revision of some anomalous great vessels was done because of the possibility of a tracheal obstruction as suggested by an angiocardiogram. This, too, was of no avail. We discovered that all the attacks were precipitated by visceral stimulation (e. g., feeding, regurgitation), and that this was followed by a type of convulsion responding to routine

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anticonvulsive therapy but different from idiopathic epilepsy in that they were apparently of reflexogenic origin. Thus, avoidance of visceral (e. g., esophageal) stimulation at one end of the reflex or depression of the efferent center (e. g., cerebrum) at the other end resulted in complete relief of symptoms.

The second patient (Case 2), also 2 months of age, had similar symptoms, but no other physical abnormality was ever detected. Fortunately, she escaped elaborate and unnecessary diagnostic procedures, but she was still hospitalized for six months with a tracheotomy. Eventually an unusually sensitive carotid sinus reflex followed by heart block was demonstrated. Since we suspected that an overactive or abnormal vagal reflex was the basic problem, we achieved complete relief of symptoms by using atropine.

It is our belief that the chief difficulty with these two infants and the others discussed in this paper is due to a basically similar neurogenic mechanism. Some type of visceral stimulation (and possibly somatic) results in afferent impulses reaching the central nervous system. From here efferent impulses may stimulate an epileptogenic focus, the respiratory center or the vagus, thus causing a convulsion or respiratory and cardiac slowing with laryngeal symptoms. Which of these is the primary insult producing the general symptoms described above is obviously quite difficult to appreciate clinically. Therapeutically, at least, we have obtained excellent results by avoiding visceral stimulation or by medication directed at lessening the response of the efferent mechanism. Complete case summaries are included for the interested reader.

REPORT OF CASES

Case 1.—M. B., a baby boy, was admitted to the University Hospital at the age of 2 months, on Sept. 11, 1950, with a chief complaint as described in a letter from the referring physician of "choking when feeding, noisy breathing, and harsh cough of six weeks duration." Labor and delivery had been uneventful, and the baby weighed 6 lb. 4 oz. (2,835 gm.) at birth. The mother noted noisy breathing "like snoring" at about one week of age, especially with feedings. At about 3 weeks of age he started to have attacks from one to three times daily, "after feeding," of throwing the head back and gasping followed by cyanosis with occasional "stiffness," but no clonic movements were noted. The appetite was good, but occasionally feedings were very slow. Vomiting had occurred several times after feeding. Many formula changes were without success, and three x-ray treatments for an "enlarged thymus" caused no improvement. Admission to the local hospital for fluoroscopic and roentgenographic examinations revealed an area of pneumonia, thought to be due to aspiration, in the right lower lung field. There was also evidence of "narrowing of the trachea at the thoracic inlet." Barium swallow studies were negative. There was no history of fever or respiratory infections. The family history was noncontributory, except that one sibling at the age of 2 days had died as a "blue baby."

The baby weighed 9 lb. 7 oz. (4,280 gm.) and had a head circumference of 14½ in. (36.8 cm.), a chest circumference of 14 in. (35.6 cm.), and a height of 23 in. (58.4 cm.). On examination at the University Hospital, the infant appeared well developed and well nourished. A slight wheeze was noticed on inspiration and expiration when the baby was resting quietly, but when excited and after a feeding there was a "barking" cough with almost each breath, and expiration seemed labored. Lungs were clear to ausculation and percussion prior to feeding, but during attacks of stridor loud rhonchi could be heard bilaterally. Other physical findings included a soft systolic murmur at the left sternal border and in the pulmonary area but no other evidence of significant cardiac disease. There was a telangiectatic hemangioma 1 cm. in diameter over the left cheek, and iris colobomas without associated choroidal defects were present bilaterally.

Direct laryngoscopy proved to be negative. Roentgenograms of the chest showed an inconstant narrowing of the suprathoracic portion of the trachea. It was decided that this

represented a variety of congenital laryngeal stridor, and, accordingly, the infant was sent home to receive elixir of phenobarbital. On this occasion the infant was in the hospital for nine days and had eight attacks, the majority consisting of stridor, croupy cough, and mild cyanosis after feeding.

On Oct. 24, 1950, the baby was readmitted to the University Hospital. The infant's general condition had improved, but "noisy breathing," especially after feeding, continued. One to three times daily after eating the infant had a mild cyanotic attack that cleared spontaneously, but he also had had two severe attacks that were associated with apnea and lasted on one occasion for 10 to 15 minutes. Generalized "stiffness" was again noted, but no convulsive movements occurred. Resuscitation with oxygen was necessary on both occasions.

The physical examination revealed a temperature of 101.6 F. (rectal), pulse of 188 per minute, and respirations 52 per minute. The remainder of the examination did not differ markedly from the previous admission. Attacks as described began to occur at frequent intervals, one to five minutes after feeding. They were often associated with three to five minutes of apnea that necessitated artificial respiration and oxygen. Tonic hyperextension occurred, but clonic movements were never observed during hospitalization. Many studies were now carried out. Chest films showed an atelectatic right middle lobe (this cleared on subsequent examinations) and a diffuse narrowing of the trachea to the bifurcation which could be demonstrated only occasionally on subsequent films.

Many different feeding techniques were tried: slower feedings permitting only a suck or two at a time, thickened feedings, and gavage feeding. With the latter, very few attacks occurred. There followed a three-week period of diarrhea and vomiting that terminated temporarily any further studies. During this time only three attacks occurred. Chest films were then repeated and again showed the tracheal narrowing. More films two weeks later showed no pulmonary or tracheal abnormality. A bronchoscopy revealed a 50% reduction in the size of the lumen in the lower portion of the trachea that pulsated inward with each heart beat. The esophagoscopy revealed no abnormality. It was thought that the tracheal obstruction might be due to an aberrant vessel. A tracheogram again revealed the narrowing at the level of T2, which was thought to be due to compression by unidentified vessels. An angiocardiogram revealed a right-sided position of the aorta with the arch at the level of T3. It was thought that possibly the innominate artery on the left was exerting some pressure on the anterior surface of the trachea but that there was no vascular ring present. The tracheal narrowing was considered to be due to some congenital weakness of the wall.

However, with attacks becoming more frequent, it was thought that a thoracotomy was urgently indicated if anything was to be done to save this infant's life. At surgery the left innominate artery was found to arise from the right aortic arch just to the right side of the trachea and to pass obliquely across the trachea, then to divide into the carotid and subclavian arteries. The right carotid artery arose to the right of the trachea and had no contact with it. No ductus arteriosus was found, and no retroesophageal vessel was palpable. Although there was no obvious compression of the trachea, the left subclavian artery was divided and the innominate suspended from the sternum.

Postoperatively there was no relief of symptoms during two more months of hospitalization. Belladonna drops were given for a short period without effect. Gavage feedings again became necessary at intervals in order to decrease the attacks. The infant had already had a trial of phenobarbital without success. Since the infant had been in the hospital for more than five months and we had little more to offer, it was decided to send the child home. Actually, discharge was not indicated, but, because the parents were very anxious to have him home and because they lived but a few blocks from the local hospital, discharge was carried out. However, because the attacks resembled grand mal convulsions, he was sent home on phenobarbital (0.016 gm. t.i.d.) and diphenylhydantoin (Dilantin) (0.032 gm. q.d.). An electroencephalogram (Fig. 1) prior to discharge had shown a record consistent with a convulsive disorder but not diagnostic of one. An electrocardiogram and gastrointestinal series were negative. Routine blood and urine studies repeated on many occasions during hospitalization contributed no information. The Kahn serological reaction was also reported to be negative.

Fourteen months after discharge this child had not had one attack. One month prior to his return all medication was discontinued, and a repeat EEG (Fig. 1) suggested some improve-

ment. Skull x-rays on this return visit were also negative. His intellectual and physical development appeared to be entirely normal.

Case 2.—A. V., a baby girl, was admitted to the University Hospital at the age of 2 months on Jan. 4, 1952, with a chief complaint as stated by the mother of "choking and turning blue" for the previous 24 hours. On the preceding day the infant seemed to "gasp for breath" while eating. On the morning of the day of admission the infant developed "wheezing and crowing" breathing followed by cyanosis. She was rushed to the local hospital, where periods of apnea continued to occur. In the attempt to clear the throat of accumulated mucus, "breathing stopped" with each aspiration. The infant was given respiratory stimulants, oxygen, and penicillin and transferred to our hospital. The past history was otherwise noncontributory. Birth took place precipitously after nine months' gestation. The baby weighed 4 lb. 4½ oz. (1,940 gm.), and on discharge about two weeks later weight was 5 lb. 1¾ oz. (2,320 gm.). The infant took an unboiled pasteurized-milk formula with a small amount of added granulated sugar without difficulty. No vitamins had been given. The family history was noncontributory.

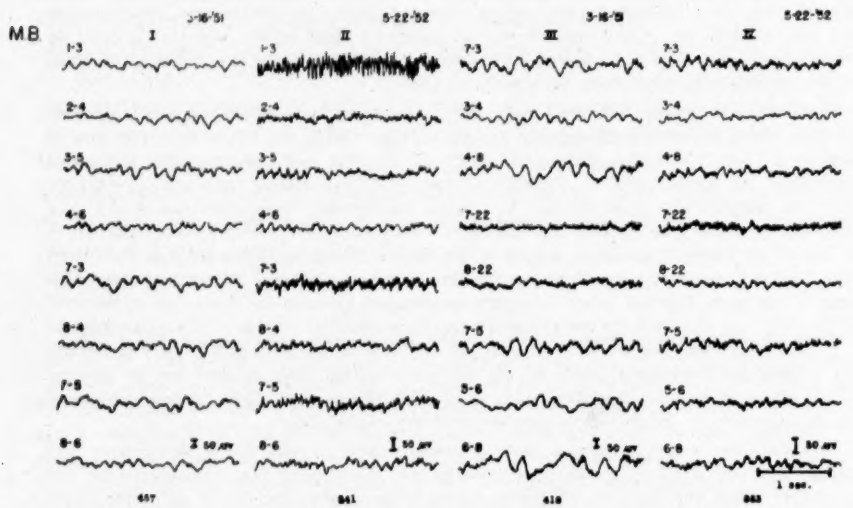

Fig. 1.—EEG taken 14 months apart, before and after the institution of anticonvulsant therapy: March 16, 1951, I and III, routine bipolar and coronal recording shows mild diffuse slow (5 to 6 per second serial and single 2 to 4 per second) waves of medium to high voltage in all areas; May 22, 1952, II and IV, improvement of the pattern. Establishment of 7- to 8-per-second waves. Fast waves (II, Strip 1) are muscle artifacts. Vertical lines represent 50 μv. calibration and horizontal line one second calibration.

Records at this age level are difficult to evaluate unless paroxysmal formations are present which are not seen here. However, the initial record was evaluated as mildly abnormal. There is a noticeable improvement in the second record, but one cannot say this is due to the medication alone; maturation may have been a factor.

On admission the infant weighed 7 lb. 4 oz. (3,290 gm.) and had a pulse rate of 126 per minute; respirations varied between 0 and 36 per minute. There were periods of normal respiration associated with periods of apnea, cyanosis, and obvious inspiratory distress. The remainder of the physical examination, including the heart and lungs, was negative. An emergency laryngoscopy and bronchoscopy was done and proved to be negative, except it was noted that with the introduction of the bronchoscope respirations ceased although cardiac activity continued. Stimulants and oxygen were necessary to institute respiration. In addition, 0.1 gm. of calcium gluconate was given intravenously without any improvement. A blood calcium level drawn prior to treatment proved to be within normal limits (9.5 mg. per 100 cc.). It was

noted that respirations seemed better when the chin was held up. Since the infant's condition was still critical, an emergency tracheotomy was done with immediate improvement. The baby was then given a course of phenobarbital for four weeks. During this time the tracheotomy tube was removed on one occasion for 55 minutes and 30 minutes on another, when symptoms of "crowing respirations" and distress appeared necessitating reintroduction of the tracheotomy tube. A chest film on Jan. 4, 1952, was negative, but another on Jan. 14, 1952, suggested a slight narrowing of the trachea immediately above the tracheotomy. A tracheogram was unsuccessful, and, because of the child's condition, no further attempts were made to visualize the trachea. Another chest film on Feb. 7, 1952, was again normal. Laryngoscopy was repeated on five occasions and each time revealed normal structure and function of the larynx.

For the next few months the child received special nursing care, and the tracheotomy was taped off at intervals without incident. However, it was later discovered that this offered no obstruction to breathing and that sufficient air could be obtained from leakage around the tracheotomy. With a stethoscope in place over the precordium, the tracheotomy was then closed with a finger, making respirations impossible except through the nose and mouth. There

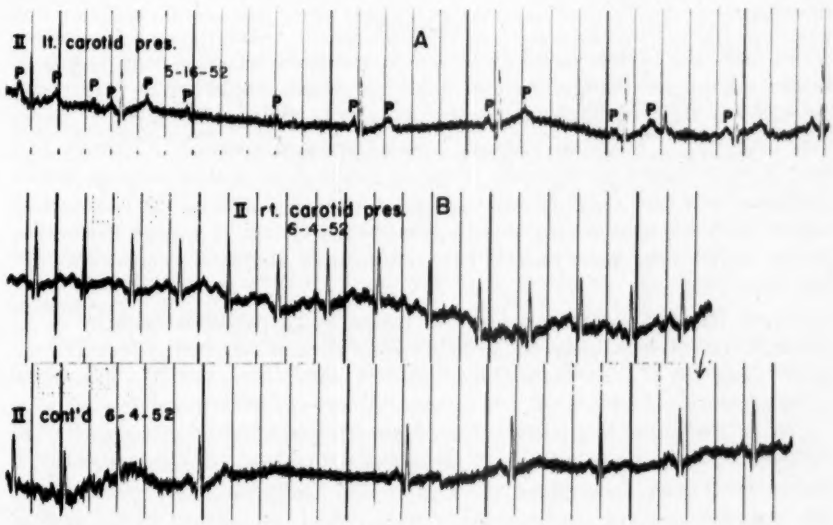

Fig. 2.—*A*, part of original electrocardiogram demonstrating marked slowing of the auricles (*P*) in Lead II in addition to partial temporary heart block. *B*, Slowing of auricles evident without heart block.

followed almost immediately a marked drop in cardiac rate from around 150 to 160 to 40 or 50 per minute. Associated with this bradycardia the child appeared dyspneic and developed perioral cyanosis and profuse sweating which all terminated with the opening of the tracheotomy. A few days later with an electrocardiograph (Fig. 2) in place the experiment was repeated; the heart rate was 165 per minute, but with obstruction of the tracheotomy and especially after left carotid sinus pressure a marked bradycardia developed. With only left carotid sinus pressure there also developed temporary A-V heart block (approximately 3:1). Clinically the infant appeared to have mild symptoms of respiratory distress as described above. A repeat laryngoscopy proved to be negative, but during aspiration of mucus in the pharynx slowing of the cardiac rate was noted. These studies offered a possible explanation for the etiology of the symptoms, and, accordingly, the baby was started on tincture of belladonna 20 minutes before each feeding. About one week later the ECG (Fig. 2) was repeated under similar circumstances when the heart rate was 188 per minute. On this occasion carotid sinus pressure (either side) and obstruction of the tracheotomy produced only a sinus bradycardia with no

evidence of A-V block or the clinical symptoms of respiratory distress. We thought, however, that there had been a clinical improvement in the child even though the inability to demonstrate A-V heart block may only have been due to inadequate stimulation of the carotid sinus. An electroencephalogram demonstrated some asynchronous activity in the right parietal area that could be compatible with an interseizure epileptic pattern, however, a recheck EEG in a few months was recommended.

Other studies while in the hospital including skull x-rays, Kahn serological testing, intradermal tuberculin tests, and routine blood and urine examinations provided no information.

Because of the apparent response to atropine the tracheotomy tube was removed. Two weeks later, during which two weeks there were no symptoms of respiratory distress and the child cried normally, though somewhat hoarsely, the infant was discharged to the care of her mother with the recommendation that tincture of belladonna, 5 drops one-quarter hour before feedings, be given four times a day. Discharge was six months after admission. The child was seen one month after discharge; she was still taking atropine and had had no further attacks. Carotid sinus pressure elicited no cardiac changes that could be detected by auscultation.

COMMENT

In 1876, the French neurologist, Charcot, described a clinical entity which he termed "laryngeal vertigo." * The following decade found many such cases described in the literature with new names such as "laryngeal epilepsy," [2] laryngeal neurosis," [3] "laryngeal syncope," [4] and "laryngeal chorea." [5] Charcot's first four cases consisted of laryngeal irritation followed by central nervous system symptoms and then rapid termination of the individual attack. These frequently started with a cough and occasionally a subjective feeling of laryngeal irritation. In the second stage some patients lost consciousness and some exhibited convulsive movements.

There followed in 1896 an excellent review of all published cases by A. C. Getchell [6] in which he found the great majority of cases occurred in men (73 out of 77), and loss of consciousness was found in many (61 out of 77). Convulsive movements were described in 21 cases and definitely mentioned not to occur in 8. In 66 of the cases the attacks occurred after a preceding coughing spell. The family history described a "nervous temperament," epilepsy, or some neurological disease in 22 cases. Descriptions as recent as 1945 [7] still leave much doubt whether this symptom complex is of epileptic origin; indeed, the authors of the original descriptions were not in agreement. In 1923, Beaman Douglas [8] described this disease in a 59-year-old man who fell unconscious during coughing attacks. This patient received phenobarbital (Luminal) in addition to local treatment to the throat and was relieved of attacks. There was little doubt in this author's opinion that this disease was the same as that originally described as "laryngeal vertigo." but he believed it was definitely an "epileptiform attack of the more severe variety of the 'petit mal' group of symptoms produced by a laryngeal irritation." Even Getchel believed that if this was not epilepsy ". . . at least there is a condition of unstable equilibrium of the central nervous system. . . ."

Thus a review of the literature provided us with only a vague and poorly understood syndrome involving the larynx and associated with central nervous system symptoms. In addition, no case in this group had been described in infants or children until the case report by Mercer [9] in 1945. The latter provides the background for what we now believe to be a distinct clinical entity, and so we

* Charcot, cited by McBride.[3]

have quoted excerpts below from this original article. The report concerns a newborn infant with a tracheoesophageal fistula who was operated on a few days after birth.

During the first two postoperative days there were several periods of apnea and cyanosis, which were readily relieved by stimulants, artificial respiration and inhalations of oxygen and carbon dioxide. On the third postoperative day, small feedings of dextrose were started orally, and, although respirations were noisy throughout feedings, no serious disturbances of respirations occurred. Starting on the twelfth postoperative day, this patient began to have increasingly severe episodes of stridorous respirations coming on during or shortly after feeding. These became severe enough to cause cyanosis. On the forty-seventh postoperative day, they were for the first time accompanied by cardiac and respiratory arrest. This particular attack started as usual, when after a feeding the infant began breathing noisily and appeared apprehensive. Breathing rapidly became more difficult and stridorous, similar to that which occurs with acute laryngeal edema, and all the accessory muscles of the respiration were brought into play. In a few minutes the infant became cyanotic, and suddenly all respiratory attempts ceased in the expiratory phase. She became limp, and no pulse was discernible. It was thought that she had died, but, nevertheless, strenuous attempts at resuscitation were carried out. These included artificial respiration, inhalations of oxygen and carbon dioxide, pharyngeal suction and injections of nikethamide and caffeine. After about two minutes, during which there was no evidence of respiratory or cardiac activity, the infant finally vomited, passed a loose stool and began breathing. At this time the pulse was rapid and thready. Respirations were noisy and moist and continued so for about two hours. The pulse rate rapidly returned to normal. . . .

When gavage feeding was instituted, there was a considerable diminution in the number of severe attacks, but the lesser episodes of stridor continued. She was given a trial of atropine sulfate in the form of 1 drop of a 1:2,000 solution (approximately 0.00003 Gm.) ten minutes before each meal. Following the addition of this small dosage of atropine, there was a noticeable diminution in the lesser episodes. These recurred when atropine was discontinued three weeks later.

More cases have since presented themselves of infants who, having congenital dysplasias involving mediastinal structures, develop periods of noisy breathing associated with apnea and cyanosis for no apparent reason. Brief case histories of two such problems encountered in the past three years are presented below. These infants had tracheoesophageal fistulae repaired surgically, and preoperative symptoms leading to the diagnosis were similar in each.

Case 3.—S. P. N., a baby boy, was operated for a tracheoesophageal fistula three days after birth and did well postoperatively. On the first postoperative day he became cyanotic while being suctioned. On the 10th postoperative day, following a transfusion of whole blood, respirations slowed and almost ceased, except for an occasional gasp, over a period of 15 minutes. Epinephrine, 0.1 cc. I.M., caused no change. No heart sounds could be heard and there was no pulse. Epinephrine, intracardiac injection of 0.1 cc., and artificial respiration with oxygen were continued. The infant was intensely cyanotic. Then suddenly respirations appeared and with increasing crescendo returned to normal. Heart sounds reappeared and the infant made a full recovery. There was a mild episode of cyanosis on the 25th postoperative day when passage of a string for future dilations was attempted. Also, on the 35th hospital day he became cyanotic after regurgitation of a feeding. Although later he developed a leak at the operative site, he was discharged well on the 68th day after admission. However, it was necessary for him to return for future esophageal dilations.

Case 4.—D. K., a baby boy, was operated for a tracheoesophageal fistula on the second day of life. On the second postoperative day respirations became rapid, and the infant turned cyanotic. There was some improvement after aspiration of the mucus. He had a second attack the same day with labored respirations and did not seem to improve with the administration of oxygen. Laryngoscopy failed to demonstrate an abnormality. The infant was then given 0.0001 gm. atropine hypodermically every 4 hours for 24 hours, and no further attacks were

noted until the sixth postoperative day, when a pneumothorax was found on a chest roentgenogram. With further treatment the infant steadily improved until two and one-half months after surgery when, during a transfusion, he developed a period of apnea that lasted about five minutes and was associated with severe cyanosis. The infant recovered after artificial respiration and oxygen and had no further attacks. He was discharged in good condition about four months after admission.

Many reports have established that autonomic reflexes can produce cardiac and respiratory irregularities. In one report, a 6-year-old boy developed cardiac arrest following adenoidectomy.[10] The symptoms recurred with nasopharyngeal packing but could be completely prevented with the use of atropine. Cardiac and respiratory irregularities, developing during anesthesia, have also been shown to be the result of mechanical stimulation of the tracheobronchial tree and are presumably due to vagovagal reflexes which can be depressed with atropine.[11] Experimental studies in dogs suggest that reflexes originating within the muscles of the mouth, tongue, trachea, and esophagus, when put on a stretch, stimulate the cardiac and respiratory rate.[12] Thus it would seem that these reflexes can either cause a depression or acceleration of cardiac and respiratory rates. Some adults have developed Adams-Stokes syncope from complete heart block due to sensory irritation of the vagal afferent fibers.[13] In one of the cases presented, attacks were precipitated by inflation of a balloon in the region of a small esophageal diverticulum and abolished by the use of atropine. Similar attacks precipitated by eating were characterized by pallor, hoarseness, slowed cardiac rate, and unconsciousness. A second patient developed attacks of syncope following stimulation of a localized area in the pharynx by swallowing, and these were abolished by the use of atropine. However, since the response to atropine is variable, these authors suggest this may depend on whether the reflexes are cardioinhibitory or vasomotor. Depending on which reflex is most active, cardiac slowing may precede or follow the early symptoms of Adams-Stokes syncope. In patients in whom symptoms of syncope and convulsion were precipitated by carotid sinus pressure, atropine was effective only in those cases where the symptomatology depends on asystole or a slow cardiac rate.[14] However, epinephrine temporarily abolished the signs and symptoms regardless of which reflex was most active. Their evidence indicates that the motor stimulation of the vagus depends in the majority of cases on reflex stimulation rather than local stimulation of the vagal endings and that three main types of responses can be illicited: (*a*) cardiac slowing or asystole, with or without a decrease in blood pressure; (*b*) a fall in blood pressure without cardiac slowing; (*c*) cerebral circulatory changes, without a slowing of the heart or a change in the blood pressure.

In our series of patients there was evidence of an overactive autonomic reflex. None of the infants demonstrated organic disease that could explain their symptoms. The presence of what appeared to be a "trigger mechanism" initiating attacks separated these infants from the more familiar group of "idiopathic epileptics." In the first infant, M. B., elaborate attempts to establish a diagnosis by the referring physician and on our pediatric service failed. The thymus was not "enlarged" and the larynx was perfectly normal on repeated examinations. Since a vascular anomaly was suspected of causing tracheal compression, surgery was undertaken on the 116th day of hospitalization. A left innominate artery was found, but apparently it was not causing much tracheal compression. Nevertheless, the vessel was tacked to the sternum after the left subclavian artery was divided as recommended by

Dr. Gross.[15] The attacks persisted in spite of surgery and seemed to be definitely related to feedings; the only alteration in feeding technique that resulted in almost complete relief was the use of gavage feedings. He was fed by gavage for 42 days at various intervals out of 168 hospital days. Ninety-three per cent of the attacks occurred during the periods of nipple feeding, and the remaining six attacks were either very "mild cyanosis" or occurred following an emesis of the gavage feeding. Probably regurgitated food can as easily set off the "trigger" as swallowed food. These facts led us to believe we were dealing with an unusually sensitive autonomic reflex with a "trigger area" somewhere in the upper gastrointestinal tract. Unfortunately, we were not able to demonstrate any other excessive vagal sensitivity in this infant by stimulating the pharynx with a tongue blade, by inflating a latex balloon in the esophagus, or by pressure on the carotid sinuses. The location of the "target area" is even more difficult to postulate. However, it is interesting to note that one of the periods of greatest freedom from symptoms while in the hospital was during a bout of diarrhea and vomiting when there was mild superimposed acidosis as substantiated by blood acid-base studies, and the subsidence of convulsive symptoms in the presence of acidosis is well known. Ultimately an electroencephalogram presented findings compatible with a convulsive disorder.

The authors are of the opinion that this was not a simple convulsive disorder for several reasons. This infant had severe laryngeal stridor followed by cyanosis and apnea, and only then did the appearance suggest a convulsion. Second, both infants could easily be relieved of symptoms by avoiding apparent "trigger areas" without treating the convulsions in one case and the stridor in the other. Since it was not feasible to consider gavage feedings for the rest of the infant's early life and because every other approach had been exhausted, it was decided that his symptoms might stem from convulsions precipitated through a trigger area somewhere in the pharynx or esophagus. Phenobarbital alone had failed, so it was now combined with diphenylhydantoin, and then, by what appeared to be significant abruptness, no further attacks occurred for 14 months (period of follow up).

A. V. presented a similar problem, but because of severe laryngeal obstruction a tracheotomy was done. Later investigation proved that with obstruction of the tracheotomy the infant developed laryngeal obstruction along with other central nervous system manifestations, namely, bradycardia, pallor, and profuse sweating. We were thus able to demonstrate a sensitive vagal mechanism that conceivably could be the source of the laryngeal stridor and that seemed to respond to the administration of atropine. This permitted the removal of the tracheotomy and the discharge of the infant. One month later this infant still had no further difficulty.

The last two patients (Cases 3 and 4) typify some of the problems encountered after the surgical repair of a tracheoesophageal fistula. Many of these infants have stormy postoperative courses with aspiration of mucus or gastrostomy feedings; some develop severe pneumonia that is difficult to clear because of constant contamination from aspiration; in others a leak may develop at the operative site or even a spontaneous pneumothorax or hemothorax. Although not all attacks of cyanosis, associated with apnea and occasional cardiac standstill occurring in these postoperative infants, can be attributed to some mysterious vagal or autonomic reflex, many such episodes are not easily explained otherwise. Here, too, autonomic reflexes appear to be important in producing symptoms through "trigger areas"

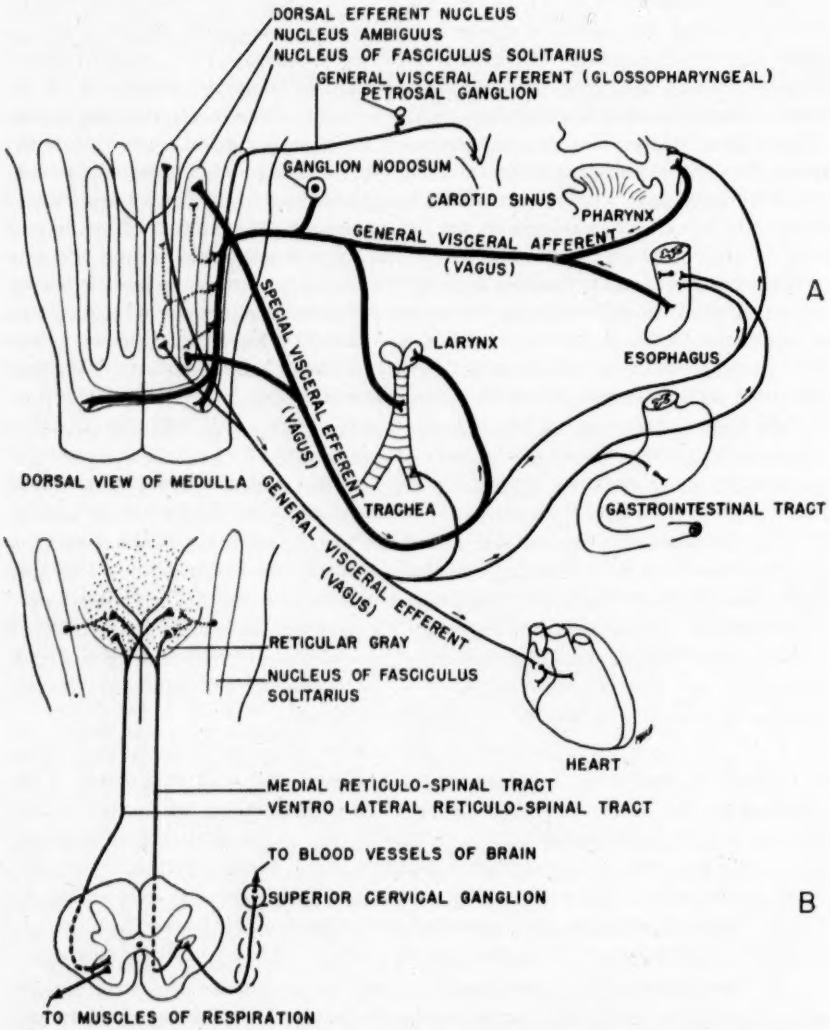

Fig. 3.—*A*, schematic representation of the neuroanatomical pathways involved in vagal reflexes. Major afferent and efferent connections of the vagus and glossopharyngeal nerves. *B*, efferent connections from the reticular formation to the muscles of respiration and sympathetic nerve centers.

somewhere in the upper respiratory or gastrointestinal tract. Possibly the presence of some mediastinal dysplasia predisposes to such attacks. We now believe this neurological abnormality may occur not only as a sequela of surgery for tracheoesophageal fistula but also in an otherwise normal infant. Occasionally the ability to demonstrate other sites of vagal sensitivity may aid in the diagnosis. Carotid pressure illicited definite signs of vagal activity in our second patient (Case 2), and although this may be a normal phenomenon, we believe it suggests in this case that the presenting symptoms of stridor and apnea are of reflex vagal origin. Others have reported a similar relationship; one adult developed syncope not only after stimulation of a sensitive area in the pharynx but also following pressure over the vagal sheath and the left eyeball.[16] On the other hand, M. B. (Case 1) had no other sites of vagal sensitivity, although he responded to treatment directed at an abnormal reflex.

The relationship of pharyngeal, tracheal, or carotid sinus stimulation to laryngeal obstruction in these patients is difficult to understand unless it is of neurogenic origin. Examination of the accompanying diagram (Fig. 3) will give the reader some idea how these reflexes are mediated through normal neuroanatomical pathways. No attempt has been made exhaustively to describe the anatomy of this portion of the central nervous system, since many details are not fully understood. We wish to emphasize the interrelationships of the many cranial nerve nuclei and the reticular cell formations which permit transmission of afferent impulses to efferent centers; these then stimulate or inhibit various end organs important in the neurogenic reflexes described above.† Thus afferent impulses from the carotid sinus, pharynx, esophagus, or trachea may produce laryngeal symptoms or changes in cardiac or respiratory rhythm. Connections to the bulbar reticular formation permit control of the muscles of respiration and of sympathetic centers through descending pathways. Although it is possible now to understand the mode of transmission of these afferent impulses, the underlying cause of the increased sensitivity of these reflexes in some infants is unknown. There is still a great deal to be learned about this syndrome. At this point, we have only clinical interpretation of symptoms at one end and clinical response to treatment at the other to encourage us to believe that some abnormalities in function of the cardiovascular and respiratory systems may be caused by neurogenic reflexes that are remedial to simple clinical procedures.

SUMMARY AND CONCLUSION

We have presented the case histories of several infants whose symptoms of respiratory embarrassment were apparently due to overactive autonomic reflexes rather than to organic obstruction. These reflexes may cause stridor, respiratory and cardiac depression, or even convulsions. They seem to arise in the upper respiratory and gastrointestinal tracts. The alleviation of symptoms in the first baby (M. B.) by gavage feedings suggests a neurogenic "trigger" mechanism. The relief of symptoms during acidosis and by anticonvulsive drugs implies a "target" area somewhere in the central nervous system. In one patient who was otherwise perfectly normal (A. V.), we were able to induce symptoms identical to those necessitating hospitalization by a path (carotid sinus stimulation) apparently not related to the original "trigger" areas. Also, infants with esophageal and tracheal dysplasia

† References 17 and 18.

which results in atresia, fistulas, etc. seem predisposed to the development of respiratory and cardiac symptoms that frequently can only be explained on the basis of a neurogenic reflex.

It appears that there are distinct similarities between the symptom complexes of all these infants: 1. Visceral stimulation, such as the passage of food through the esophagus, seems to be the initial insult leading to central nervous system symptoms. 2. Each infant presented varying degrees of laryngeal stridor preceding cyanosis. In no case were we able to demonstrate a structural abnormality of the respiratory tract that could explain the stridor. 3. The end organ was variable; in the first patient the cerebrum was affected, and in the remaining infants the cardiac and respiratory centers. 4. Therapy was successfully directed at various points of these reflex arcs by (*a*) avoiding the visceral stimulation which presumably acts as a "trigger" in intiating attacks, (*b*) depressing the cerebral "target" area by anticonvulsive therapy, and (*c*) depressing vagal activity with atropine.

The age of the patients and the severity of the symptoms precluded any scientific attempts to prove the exact site of the trigger area or the manner through which such symptoms were mediated. However, experimental evidence and reports of diseases which seem to fall under this general classification of reflex origin suggested the diagnosis. More emphasis, then, should be placed on such origin of symptoms, since it offers a valid, though not yet fully understood, mechanism for the causation of symptoms which even in these cases were earlier classified under the more vague groupings of "thymic enlargement" and "congenital laryngeal stridor." Whether apnea with cyanosis, stridor, cardiac arrest, or even convulsions will be the end point of the abnormal autonomic channel depends on the structure of the reflex. Only time, observation of more cases, and more detailed clinical investigation will supply the answers.

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Dr. Elizabeth C. Crosby assisted with neuroanatomical concepts. Dr. F. D. Johnston and Dr. B. K. Bagchi interpreted the electrocardiographic and electroencephalographic findings.

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Case Reports

MECONIUM PERITONITIS DUE TO INCARCERATED MESENTERIC HERNIA

Recovery Following Operation for Intrauterine Rupture of Intestine

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PERFORATION of a portion of the gastrointestinal tract may occur during intrauterine life, at the time of delivery, or in the neonatal period. The term "meconium peritonitis" commonly designates the inflammatory response to soiling of the peritoneal cavity by the constituents of the meconium, chemically of a highly irritant nature and bacteriologically sterile for a short and variable period after birth. The chemical peritonitis thus induced becomes an even more serious problem when bacterial contamination is added.

The majority of the cases of meconium peritonitis are secondary to intestinal obstruction, gangrene, and perforation caused by a congenital lesion, such as malrotation of the bowel with adherent bands and/or volvulus, atresia, meconium ileus associated with pancreatic fibrosis, duplication of the bowel, or strangulated inguinal hernia. Trauma at the time of delivery has been implicated by some, and in many instances neither a competent producing cause nor actual site of perforation has been found.*

The number of reported cases of meconium peritonitis in which operation resulted in survival is small. Surgery has been performed, in most of these at some time between the first and sixth days after delivery: Forshall and co-workers, 10 hours [6]; Conrad and Robbins, 22 hours [5]; Gover, 24 hours [10]; Arnheim, 28 hours [2]; Standard, 44 hours [24]; Gross, 50 hours (reported by Neuhauser [18]); Packard and Reynolds, 48 hours plus "a few" [19]; Moretz and Morton, 52 hours [17]; Agerty and co-workers, 56 hours [1]; Duncan and co-workers, 60 hours [7]; Lee and MacMillan, 65 hours [14]; May and Brintnall, 3 days [16]; Brunkow and co-workers, 4 days [4]; and Low and co-workers, 4 days.[15] We have not found reports of successful operations prior to 1943.[26] The case of Biggs and Pontius, operated on at 8 days of age, does not fit into the category under discussion.[8] Meconium peritonitis associated with meconium ileus and fibrocystic disease of the pancreas has uniformly been fatal.†

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* References 4, 19, 21, and 24.

† References 11 and 12.

It is not possible to state definitively how many of these 14 infants surviving after operations performed for meconium peritonitis in the first five days after delivery sustained the bowel perforation during intrauterine life. Marked abdominal distention noted immediately upon birth of the baby, as in the present instance, and followed promptly by exploration provides the most convincing proof. The abdominal enlargement may be so marked as to interfere with a normal delivery.[22] Distention at or within a few hours of delivery was recorded in only 5 of the 14 successful cases above.‡

While calcification may develop rapidly in meconium free in the peritoneal cavity, this finding and/or the demonstration of calcium deposits in the wall of

Summary of Cases of Meconium Peritonitis Operated on, with Survival

Authors	Age at Time of Operation	Etiology	Operative Procedure
Forshall and others, 1952 [6]	10 hr.	Volvulus of ileum (bands ?)	Resection and anastomosis, one-stage
Conrad and Robbins, 1951 [5]	22 hr.	Atresia of jejunum	Resection and anastomosis, one-stage
Gover, 1950 [10]	24 hr.	Not stated	Suture of perforation
Arnheim, 1945 [2]	28 hr.	Atresia of ileum	Staged operations; resection and anastomosis
Standard, 1952 [24]	44 hr.	Rectosigmoid ? cause	Transverse colostomy; closed later
Neuhauser (Gross), 1944 [18]	50 hr.	Atresia of jejunum	Anastomosis
Packard and Reynolds, 1951 [19]	48 hr. ("plus a few")	? trauma ? sigmoid	Drainage of abdomen
Moretz and Morton, 1950 [17]	52 hr.	Volvulus of small intestine	Resection and anastomosis, one-stage
Agerty and others, 1943 [1]	56 hr.	? plug of meconium	Suture of perforation in ileum
Duncan and others, 1943 [7]	60 hr.	Multiple small bowel atresias	Excision and anastomosis, one-stage
Lee and MacMillan, 1950 [14]	65 hr.	Atresia of transverse colon; ruptured cecum	Staged operations
May and Brintnall, 1952 [16]	3 days	Mesenteric hernia	Resection and anastomosis
Brunkow and others, 1949 [4]	4 days	Not identified	Drainage of abscess
Low and others, 1949 [15]	4 days	Atresia of ileum	Anastomosis
Authors' case, 1949	2½ hr.	Mesenteric hernia	Staged operations

the resected bowel are highly suggestive of intrauterine perforation. In addition to the present case, calcification was demonstrated histologically in specimens from four of the infants surviving after operation.§ The demonstration of irregular plaques of calcification on a roentgenogram, as described by Neuhauser,[18] has also been reported by others.‖

It is, therefore, reasonable to accept on the basis of the criteria above 9 of the 14 previously reported cases surviving after operation for meconium peritonitis as having perforated in utero.¶ The operations have varied from simple drainage of the abdomen or suture of the perforation to complicated resections and anastomoses in stages (Table).

‡ References 2, 8, 10, 14, and 19.
§ References 2, 8, 15, and 18.
‖ References 2, 4, 5, 10, and 15.
¶ References 2, 4, 5, 8, 10, 14, 15, 18, and 19.

Transmesenteric hernias constitute one of the less common causes of intestinal obstruction. Prolapse of a portion of the bowel may take place through a mesenteric aperture, with subsequent incarceration, volvulus, and gangrene. The defects in the mesentery are presumed to be of congenital origin and may occur in a variety of locations. Cutler and Scott [6] analyzed a series of 50 cases and found the defects situated as follows: ileocecal junction, 35; midileum, 6; jejunum, 2; mesosigmoid, 1; multiple, 1; unspecified, 5. The subject has been reviewed most recently by Pomeranz and Steppacher.[20]

The reported cases of transmesenteric hernia have ranged in age from 32 hours [23] to 88 years.[25] No attempt has been made to assemble separately the cases coming to surgery in the neonatal period. Ladd and Gross [13] describe three instances in children with one death; the ages are not given. They state that herniation through the mesentery is second in frequency only to diaphragmatic hernia among the internal hernias of childhood. Glover and Barry [9] summarized 47 cases of intestinal obstruction in the newborn, of which 5 were due to internal herniation. A true transmesenteric hernia was described in one instance (Case 27), with a successful operation at 5 days of age. In Cases 30 and 47, herniation of the bowel into but not through the mesentery was found. The mortality rates reported for operations for mesenteric hernias range from 15 to 50%, with death due mostly to peritonitis associated with gangrenous bowel.

Subsequent to the presentation of this material, a case report has appeared describing a successful operation for strangulated transmesenteric hernia in the neonatal period.[16] An erythroblastotic infant survived a one-stage resection and anastomosis, performed at 3 days of age, for a gangrenous segment of jejunum with peritonitis. The operation was done on April 17, 1952, almost three years after the current case. There is a striking contrast in the postoperative courses of these infants; the latter baby presented none of the problems secondary to intestinal malfunction.

REPORT OF CASE

J. B. was born at the New York Polyclinic Medical School and Hospital on July 1, 1949, at 4 p. m. after a 40-week period of gestation. The mother was a primipara, and the prepartum and family histories were negative. A double footling breech presented: delivery was further complicated by a nuchal left hand and a markedly dilated abdomen. To facilitate extraction of the after-coming head with Piper forceps it was necessary to fracture the left arm.

Physical examination immediately after birth revealed a well-developed white male infant who weighed 7 lb. 6 oz. (3,345 gm.) and was 20 in. (50.8 cm.) in height. There was evidence of a simple transverse fracture of the left humerus. The abdomen was markedly distended, suggesting the presence of both fluid and air in the peritoneal cavity. The superficial veins over the abdomen were markedly dilated and tortuous. There was no meconium in the lower bowel, and rectal irrigation was returned clear.

A diagnosis of fetal peritonitis with ruptured viscus due to a meconium ileus was made. The fractured arm was immobilized over a bass-wood splint. Laparotomy was performed two and one-half hours after delivery (E. S. H.). The peritoneal cavity was entered through a left mid-rectus muscle-splitting incision. It was occupied by a large amount of fluid and semisolid meconium of a dull greenish color. There were adhesions between numerous loops of small bowel. The proximal loops of jejunum were greatly dilated to a point where the distal jejunum had herniated thru a defect in the mesentery of the upper ileum. The herniated segment, measuring about 12 in. (30.5 cm.) in length, was twisted in a volvulus of 180 degrees. It was gangrenous and necrotic and presented a large perforation in one wall (Fig. 1). Much of it hung freely in the peritoneal cavity like wet-shredded newspaper. The ileum, distal to the gangrenous jejunum was of the caliber of a lead pencil, was coiled in small loops, and felt

irregularly solid due to inspissated pellets of meconium. The jejunum and proximal ileum were divided at the point of herniation and the gangrenous segment resected. The proximal loop of the jejunum and the most proximal point of viable ileum were brought out through a McBurney incision in the left lower quadrant, with a spur between. The left rectus incision was closed with buried on-end figure-of-eight mattress sutures of No. 35 steel wire through fascia, muscle, and peritoneum, with interrupted nonabsorbable surgical sutures (silk) for the skin. Two Penrose cigarette drains were placed at the site of the gangrenous bowel (Fig. 2).

Microscopic examination of the resected gut showed mucosal ulceration and necrosis, with edema, hyperemia, hemorrhage, and scattered areas of calcification in the mucosa and submucosa (Fig. 3).

The preoperative diagnosis of fetal peritonitis with a ruptured viscus was substantiated by the findings at operation. The meconium, free in the peritoneal cavity, did not have the green-black sticky tarry consistency characteristic of meconium ileus associated with pan-

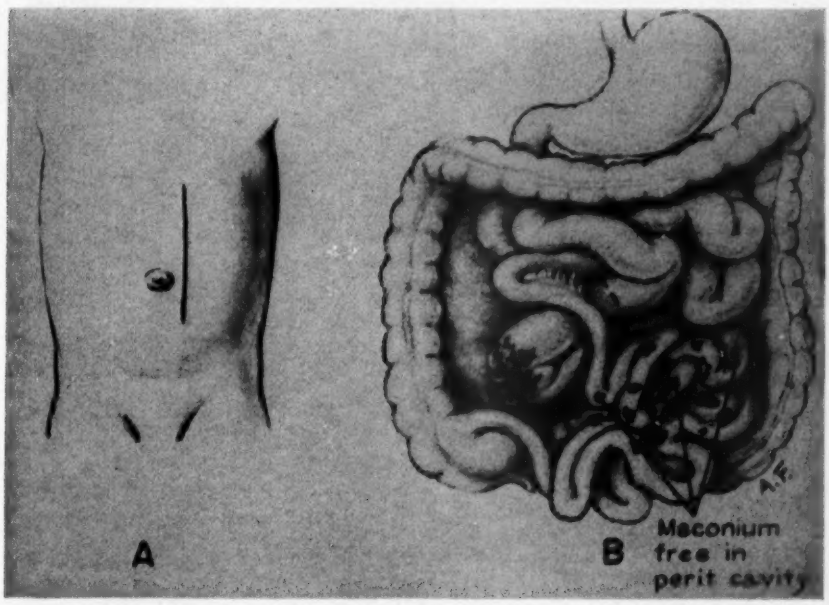

Fig. 1.—Artist's reproduction of findings at first operation. The dotted line in *B* represents a line of transection of the herniated loop of small bowel.

creatic fibrosis. Rupture of the infarcted bowel, proximal to the mechanical obstruction, had occurred a considerable time prior to the birth of the infant. Inspissation of the meconium, distal to the obstruction, was associated with the deprivation from the lower small bowel of the pancreatic, biliary, and upper intestinal secretions.

During the next four days the patient received supportive therapy consisting of transfusions and dextrose in saline by vein and subcutaneously. His general condition remained surprisingly good. Streptomycin and penicillin were administered liberally, and oxygen was given almost continuously. Irrigations of the ileum and rectum with a 1% solution of pancreatin produced large quantities of inspissated meconium plugs. Iodized oil (Lipiodol) introduced into the ileum and rectum indicated a patent lower bowel. Optimally, one would have preferred to wait until all the fecaliths in the lower segment could have been removed before risking an intestinal anastomosis, particularly in the face of such a generalized chemical peritonitis. However, because of the overwhelming mortality rate associated with high small-bowel fistulae, it was mandatory to reestablish intestinal continuity as early as possible.

On July 5 the second-stage operation was performed. The peritoneal cavity was entered through a lower right-rectus muscle-splitting incision. As a result of the preexisting peritonitis, the serosal surfaces of the bowel were edematous, and numerous adhesions were present. The exteriorized loop of jejunum was identified and transected, leaving a 3-inch (7.6 cm.) segment still protruding from the left McBurney incision. The distal end was inverted. The proximal end was inverted with an over-and-over continuous suture. The exteriorized loop of ileum was similarly treated. A perforation was identified near the line of transection of the ileum, presumably due to trauma from the irrigations, and a 6-in. (15.2 cm.) segment resected. The distal end of the ileum was closed with a continuous suture. A side-to-side jejunoileostomy was performed, using interrupted nonabsorbable surgical sutures for the serosa and a continuous Connell suture of chromic absorbable surgical suture (catgut) for the mucosa.

The caliber of the ileum had increased about threefold since the first operation. The bowel still contained a large number of hard pellets, and as many of these as possible were extracted from the open end of the elium. At the conclusion of the operation the anastomosis admitted

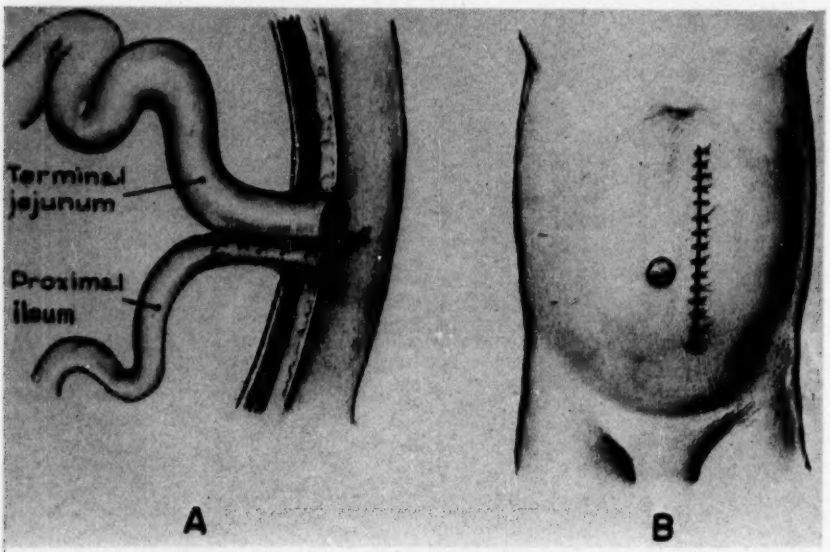

Fig. 2.—Diagram showing double-barrelled enterostomy, exteriorized through a left McBurney incision.

two finger tips. Small tears in the serosa of the ileum, secondary to milking out inspissated plugs of meconium, were repaired with interrupted nonabsorbable surgical sutures. The abdominal closure was similar to that at the first operation, but without drainage (Fig. 4).

It was felt that survival of the patient depended on his ability to propel the remaining inspissated meconium through the lower ileum before the anastomosis might be subjected to such pressure that it would give way.

For the next 10 days there was little apparent progress. Plasma and dextrose in saline were given frequently. A Levin tube was passed to the duodenum, and through this small amounts of glucose water were introduced, with occasional doses of pancreatin, starting on the second day. This was at first not well tolerated and there were frequent episodes of vomiting, mostly of thick bright-green fluid.

Five days postoperatively the patient expelled mucus and a little flatus per rectum. Five days later three formed pieces of mucus were passed. A dilute evaporated-milk formula with Dextri-Maltose was started on the 10th postoperative day. Two days later material resembling stool was evacuated following a rectal irrigation. On July 21, 16 days after the anastomosis

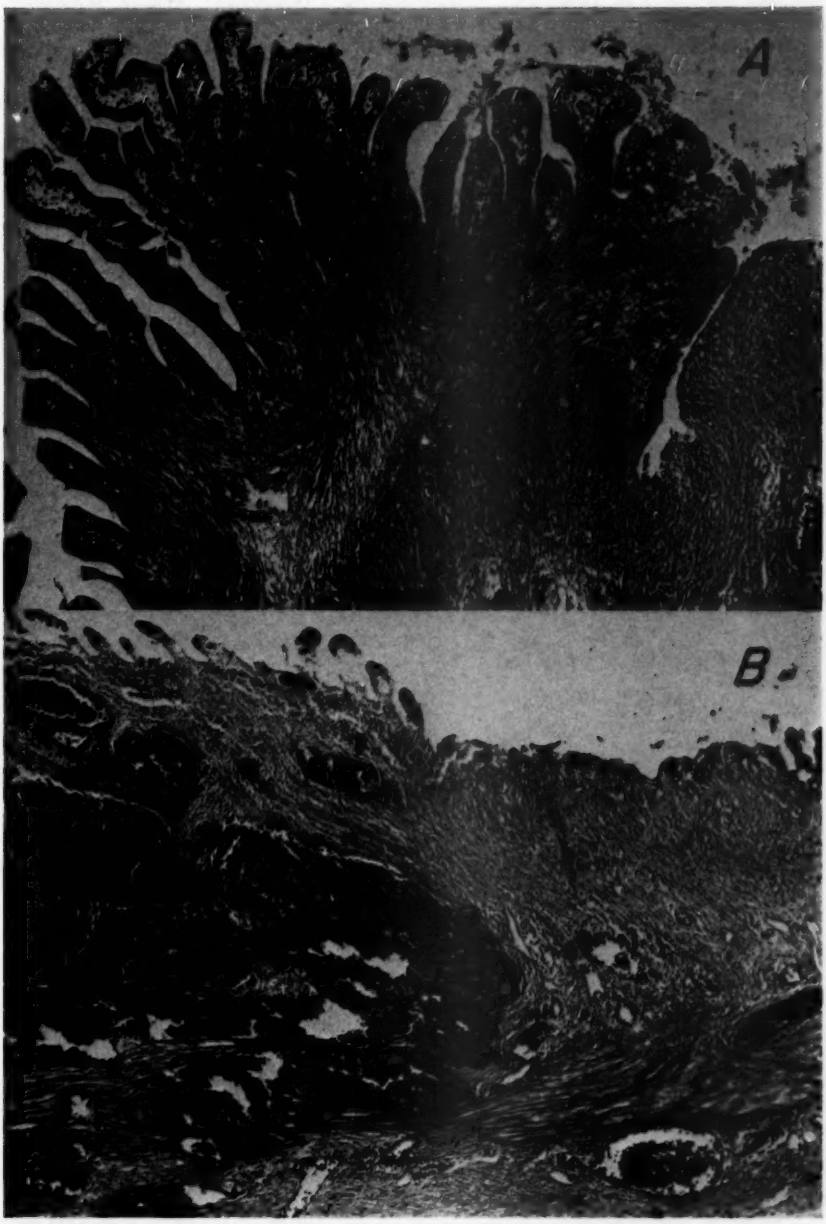

Fig. 3.—Two sections of resected small bowel, with mucosal ulceration, edema, necrosis, hemorrhage, and calcification.

and at the age of 20 days, the infant had his first normal bowel movement. His weight at this time was 5 lb. 5 oz. (2,410 gm.). Chlortetracycline (Aureomycin), penicillin, sulfadiazine, and a multivitamin preparation were given throughout this period.

Stools became more frequent, from five to seven daily, and occasionally were loose and dark green in color. A hard cough developed which was treated with aerosol penicillin. Whole milk was substituted for the evaporated milk and calcium caseinate (Casec) added. On Aug. 1 a protein milk and banana powder formula was begun. The weight was then 4 lb. 13 oz. (2,180 gm.). Four days later the weight fell to 4 lb. 10 oz. (2,100 gm.), its low point. At this time improvement began. On Aug. 17 the patient was discharged from the hospital; the weight was 5 lb. 9 oz. (2,520 gm.). There was a draining sinus at the lower end of the abdominal wound and a healing abscess in the left thigh, the site of a streptomycin injection. There was no cough, and the general condition was good. The left humerus was united and in good position.

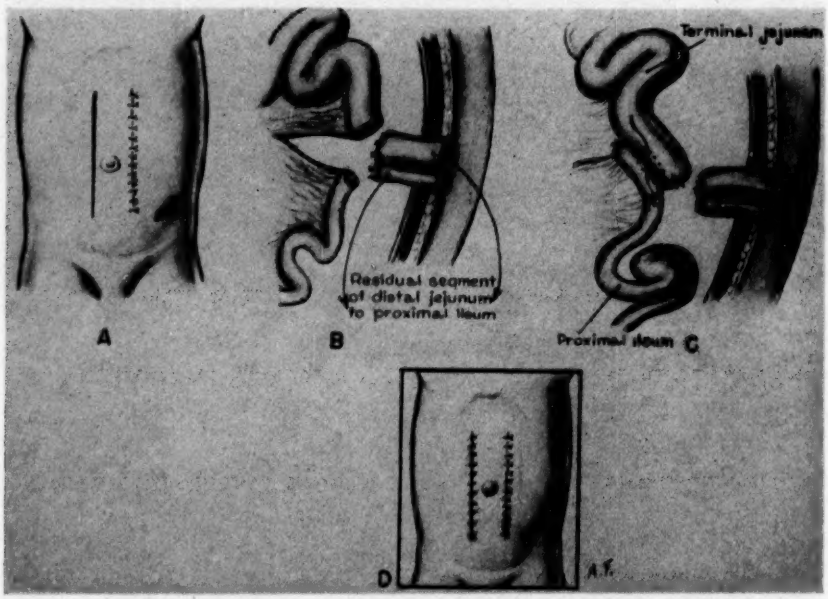

Fig. 4.—Diagram illustrating the steps in the second operation (text).

Eight days later, on Aug. 25, the infant was admitted to Babies Hospital in a dehydrated state, following a two-day period of severe diarrhea and cough. The weight was 5 lb. 7 oz. (2,470 gm.). Parenteral fluids restored his fluid and electrolyte balance. He was discharged on Sept. 9.

For the next seven weeks his general condition improved, but there was little increase in weight. During this period there were frequent stools, sometimes as many as 12 a day, but these were said to be well formed. A hacking cough responded to aerosol penicillin. On Oct. 31, aged 4 months, the weight was 6 lb. 6 oz. (2,890 gm.). Powdered protein milk formula was introduced; meat and bananas were also given. The two vertical abdominal incisions had healed well. A scant amount of mucoid secretion drained from the short exteriorized segments of small bowel.

During the next three weeks the baby gained 8 oz. (230 gm.). A gain of 5 oz. (140 gm.) in three days was noted. A severe cough then developed, followed by vomiting and diarrhea. He lost 6 oz. (170 gm.) in the next 48 hours and was readmitted to Babies Hospital on Nov. 28, aged 5 months and weighing 6 lb. 12 oz. (3,060 gm.). The infection again responded to fluid and antibiotic therapy, and he was discharged on Dec. 13, 1949.

Fig. 5.—Marantic appearance of infant at age of 6 months, weighing 7 lb. 6 oz. (7,880 gm.).

On Jan. 7, 1950, aged 6 months, the patient weighed 7 lb. 6 oz., exactly what he weighed at birth (Fig. 5). Steady improvement continued in spite of repeated attacks of furunculosis, which responded to oxytetracycline (Terramycin), and occasional bouts of coughing. At the age of one year he weighed 15 lb. 9 oz. (7,060 gm.) and was 27 in. (68.6 cm.) in length. The abdominal sinus had closed.

Growth and development were fairly satisfactory for the next year. On Feb. 23, 1951, aged 19 months, the infant was again admitted to Babies Hospital because of fecal vomiting of 24 hours' duration. A diagnosis of intestinal obstruction was made. The weight on admission

Fig. 6.—Appearance at 22 months of age, weighing 23 lb. (10,430 gm.).

was 19 lb. 3 oz. (8,700 gm.). Laparotomy was performed by Dr. Thomas Santulli. He reported a complete obstruction just distal to the anastomosis. The anastomosis was resected and an end-to-end anastomosis effected. It was estimated that a total of 3 ft. (91.4 cm.) of small intestine remained. No evidence of the previously constructed and transected double enterostomy could be found. At the time of discharge, on March 17, the wound was well healed, and the bowels were moving normally.

At 22 months of age the patient weighed 23 lb. (10.4 kg.) and was 31 in. (79 cm.) tall (Fig. 6). He was given a full, normal diet at this time, gradual substitution having been started two months earlier. A return to normal diet might have been accomplished sooner except for maternal resistance. When last seen, aged 39 months, he weighed 31½ lb. (14.3 kg.),

and was 37½ in. (98 cm.) in height. He normally had five or six well-formed stools, yellow to brown in color and foul smelling, in a 24-hour period. It was only on rare occasions that the stools were reduced to one or two a day. He appeared to have normal mental and physical development for his age.

COMMENT

The clue that resulted in prompt action in the present instance was the abdominal distention noted in the delivery room. Roentgenographic demonstration of free air beneath the diaphragm and of calcific densities in the peritoneal cavity may be of help in confirming the diagnosis of a ruptured viscus. Such evidence was not obtained in this case and should not be required prior to making the decision to operate. The abdominal percussion note is of great importance. When the generalized meconium peritonitis was found at laparotomy, it was felt that a hopeless situation prevailed, and the parents were given a most gaurded prognosis. Immediate evacuation of a huge sterile abscess before invasion by pathogenic bacteria could occur was undoubtedly a decisive factor in survival. The decision not to attempt a primary anastomosis at the first operation was obligatory, because of the impaction of the entire ileum with fecaliths of inspissated meconium. The disparity in the sizes of the bowel proximal and distal to the obstruction and the peritonitis were factors of lesser importance. Although the four days of irrigations with pancreatin solution had dislodged some of these concretions, at the time of the anastomosis the operator was dismayed to find the degree of impaction that persisted. On the other hand, the prohibitive mortality associated with high enteric fistulae in babies made restoration of the continuity of the bowel imperative.

The first normal bowel movement, at the age of 20 days, brought the first indication that the infant might possibly survive. For the next several months he exhibited an almost complete inability to assimilate food, and at the age of 6 months he presented the appearance of advanced marasmus. His clinical course during this period was strikingly similar to that observed by the operator in the case reported by Arnheim.[2] A comparable etiology was implicated, namely, loss of part of the small bowel and malfunction of the remainder secondary to the peritonitis. In neither instance could a clear-cut diagnosis of pancreatic fibrosis be established. Both babies behaved as though pancreatic insufficiency were present in the early postoperative periods, and both were treated by a celiac type of regimen. Apparently both children have compensated for this deficiency to some extent, which suggests that it may have been due at least in part to a functional depression of enzyme production or activity rather than to organic destruction of the pancreas.

At the time of the first two operations, no attempt was made to repair the mesenteric hiatus. This obviously was an error and presumably may have played a part in the intestinal obstruction that led to a third operation at the age of 19 months. Dr. Santulli described a crossing of the segments of the bowel as the cause for the obstruction. It is of interest to note that the short exteriorized segments of small bowel that had been left as a mucous fistula in the left lower quadrant, for subsequent excision, could not be identified at the time of the third operation.

Promptness in diagnosis, refusal to abandon an apparently hopeless situation, and devoted care on the part of house staff and nurses must all be acknowledged as crucial in the survival of this infant. Despite similar circumstances in other cases, death is the more usual result. When biologic tools have been developed adequate

to evaluate the additional factors that permitted this child to overcome a handicap that would have been almost uniformly fatal, an improved rate of fetal salvage may be anticipated.

SUMMARY

The successful operations for meconium peritonitis are summarized.

The successful operations for transmesenteric herniation in the neonatal period are reviewed.

A case is described in which survival resulted from staged operations for meconium peritonitis due to gangrene of the bowel incarcerated in a mesenteric hiatus hernia. The first operation was performed at the age of two and one-half hours.

This is the youngest recorded survival following operation for meconium peritonitis and the first survival in which the bowel perforation was secondary to this etiology.

Thorough examination of every newborn infant immediately after delivery, prompt diagnosis, and operation without delay are imperative if fetal salvage is to be anticipated.

Abdominal distention in the newborn is the most valuable sign indicative of rupture of the bowel in utero.

A plan of management for this condition is suggested.

ADDENDUM

Since this paper was accepted for publication, an additional case of meconium peritonitis has been reported, with survival after surgery, by Bendel and Michel (Bendel, W. L., Jr., and Michel, M. L., Jr.: Meconium Peritonitis, *Surgery* **34**:321 [Aug.] 1953.)

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ABERRANT UMBILICAL STOMACH

Report of Two Cases

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AND
R. ELMAN, M.D.
ST. LOUIS

ABERRANT gastric mucosa has been observed in many parts of the body, but it is unusual for it to be so located that a diagnosis can be made at the bedside by simply testing the clear umbilical secretion and finding that it has an acid reaction. Two such patients have been observed in the past few years.

REPORT OF CASES

CASE 1.—J. C., a 10-month-old white baby girl, was admitted to the St. Louis Children's Hospital because of a draining umbilical sinus since birth, which was premature (weight, 3 lb. 12 oz. [1,700 gm.]).

Findings on examination were negative, except for an area of moist induration about 7 mm. in diameter in the region of the umbilicus surrounded by a partly cystic, partly solid mass about 5 cm. by 5 cm. All laboratory findings were normal.

Drainage from the umbilicus consisted of a clear fluid, the amount of which did not vary with the intake of food. When tested, it turned blue litmus paper red, Congo red paper blue, thus proving the presence of free inorganic acid. The fluid was also shown to digest coagulated egg albumin. The opening of the sinus was cauterized with silver nitrate without demonstrable effect. During hospitalization an idiopathic hypochromic anemia developed, which necessitated several transfusions and iron therapy before it was corrected. Two months later, operation was performed, the procedure consisting of a transverse elliptical incision around the umbilical mass extending through to the peritoneum. The entire mass was removed. It was covered with peritoneum on its inferior surface (Fig. 1). A small Meckel's diverticulum and a normal appendix were removed before the abdominal wound was closed.

Surgical Pathology Report.—The tissue removed was an umbilical structure containing typical gastric mucosa.

The infant was discharged 10 days after operation in good condition and when last seen, four years later, was still normal in all respects.

CASE 2.—D. P., a 5-month-old white baby girl, was admitted to the St. Louis Children's Hospital because of drainage from the umbilicus since birth. For the first three months this secretion was thin and clear, and it was thought by the mother to increase during urination. At 3 months of age, the umbilicus was treated with silver nitrate, after which the discharge became more mucoid and blood-tinged. During this period there were two episodes of high fever, the cause of which remained unknown, but which subsided following the administration of sulfonamides. Family history, birth history, and development were normal.

Examination was negative except for a moderately reddened and indurated umbilicus from which a thin clear fluid escaped. There were no abnormal masses or structures felt within the abdomen or abdominal wall. Laboratory findings were all normal.

From the Departments of Pediatrics and of Surgery, St. Louis Children's Hospital.

The umbilicus continued to discharge a thin, clear fluid which when tested with nitrazine paper showed a color consistent with a pH of 4.5. At operation one week later a transverse elliptical incision was made about the umbilicus down through the peritoneum. Remnants of the hypogastric arteries and the ligamentum teres were found attached to the umbilicus. These were clamped and cut, then tied, and the entire mass removed. A very small Meckel diverticulum was noted. A normal appendix was removed. The wound was then closed in layers.

Surgical Pathology Report.—Umbilical tissue containing gastric mucosa with parietal cells (Fig. 2). Postoperative course was satisfactory, and the patient was discharged 10 days after operation. She continued to show a normal development and when last seen, five months later, was perfectly normal.

CASE 3.—The case of M. A. H. appears in the records from the St. Louis Children's Hospital. This was a 3-year-old white girl who had an umbilical cyst removed, and sections of the excised mass showed, with special mucin stains, one small area that contained definite glandular acini secreting mucus. The cyst had been present since age of 5 months, and there had never been secretion noted.

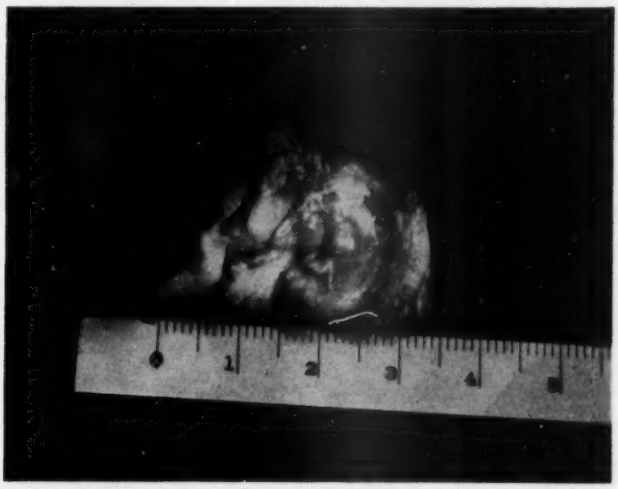

Fig. 1.—Photomicrograph of gross specimen in Case 1; the scale represents centimeters. The umbilicus can be seen on the left. Note the mucosa as shown by high-lighted area (cut cross section) in the center of the specimen.

COMMENT

In his exhaustive book on "Diseases of the Umbilicus," T. S. Cullen states, "The literature on this subject is rather scanty, but several observers have reported mucosa at the umbilicus that more or less resembles stomach mucosa." He then quotes Tillmanns, who in 1882 observed a 13-year-old boy who exhibited a tumor the size of a walnut, bright red in color and covered with mucosa, which had been present since birth. After the boy had eaten, the tumor would sometimes swell perceptibly, become redder, and the mucosa become thicker. A tenacious mucus was secreted, amounting to as much as 2 to 3 cc. in 15 minutes. As secreted, it was acid in reaction and digested fibrin in acid solution at 39 C. Chemical examination showed that it corresponded more or less closely with gastric juice. Similar cases were cited as reported by Roser, Siegenbeck, van Heukelom, von Rosthorn, all in the last century. Since 1916 there seems to have been no further reference to the subject of aberrant gastric mucosa in the umbilicus. However, in a rather complete

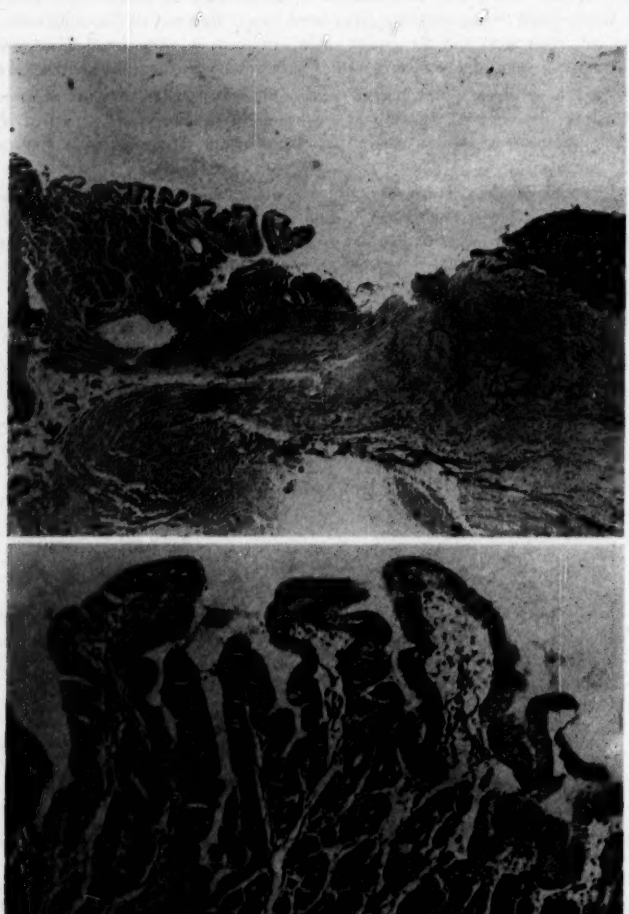

Fig. 2.—Photomicrograph of the specimen in Case 2 showing (above) the junction between normal skin and gastric mucosa with a tiny denuded area between the two, which perhaps might be called a peptic ulcer. Below is the high-power magnification showing the histological appearance characteristic of gastric mucosa.

review in 1945 Trimingham and McDonald did present a photomicrograph showing gastric mucosa in a specimen of an omphalomesenteric duct which also contained intestinal epithelium.

SUMMARY

Two cases of aberrant umbilical stomach were observed in infants who since birth were observed to have a discharge from the umbilicus consisting of a continuous clear secretion which on simple test proved to be acid in reaction. The umbilicus was completely excised and showed no connection with the gastrointestinal tract. Study of the specimens showed normal gastric mucosa.

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HYDROPS OF THE GALL BLADDER IN A FOURTEEN-MONTH-OLD INFANT

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DISEASES of the gall bladder in infancy and childhood are quite uncommon, and the presence of hydrops in an infant has rarely been encountered. Ulin, Nosal, and Martin [1] sent a questionnaire to a number of prominent surgeons about their experiences with cholecystitis and cholelithiasis in this age period, and their replies indicated that none of them had operated on children for either condition.

On the other hand, Potter [2] endeavored to demonstrate that gall bladder disease is not as unusual as general opinion would lead one to believe, and compiled a total of over 400 instances of involvement of the biliary tract in children, including 10 cases of his own. A careful survey of this large series reveals only one case which could possibly resemble the findings in the report which follows. We deem this case worthy of report because it is of the youngest child with hydrops in recorded cases, and his condition developed without symptoms.

REPORT OF A CASE

C. R., a white boy, aged 14 months, was admitted to the Jewish Memorial Hospital on Dec. 17, 1952, with a large nontender mass in the abdomen.

He was the third child of a tertipara and tertigravida mother and weighed 6 lb. 4 oz. (2,830 gm.) at birth. The pregnancy and labor were uneventful. Both parents were of Italian descent, with no history of hemolytic disease on either side. The mother had received several courses of penicillin therapy for congenital syphilis, the last given during the child's gestation. The results of her Mazzini tests were repeatedly negative.

At 15 days of age, the infant developed severe diarrhea, with marked loss of weight, dehydration, and hyperpnea. When examined the following morning, he appeared to be in circulatory collapse. He was admitted to the Morrisania City Hospital on Oct. 29, 1951, in a critical state. Examination revealed an ashen-gray pallor, sunken fontanelle, marked hyperpnea, and poor tissue turgor. Other findings were not relevant. Laboratory tests showed the following: RBC 3,390,000, hemoglobin, 8.8 gm. per 100 cc.; blood type AB positive (both parents were Rh positive); hematocrit 35%, WBC 18,000, with polymorphonuclear leucocytes 16% and lymphocytes 84%; CO_2-combining power 10 vol.% He was given plasma, whole blood, and lactated Ringer's solution intravenously and penicillin and streptomycin intramuscularly. The next day, he was somewhat improved, and the CO_2 value had risen to 70 vol.%. He continued to do well until the fifth day after admission, when marked manifestations of tetany developed, with a blood calcium value of 5.6 per 100 cc. Treatment with 20 cc. of intravenous calcium gluconate stopped the tremors. Blood cultures were negative on several occasions, and stool cultures yielded Aerobacter aerogenes, B. proteus, and Escherichia. After steady improvement, he was discharged on Nov. 18, 1951.

The infant remained well until February, 1952, when a severe bronchopneumonia developed. He was readmitted to the Morrisania City Hospital, where he received penicillin, streptomycin, and oxytetracycline (Terramycin). His response was satisfactory, and after 12 days he was sent

From the Pediatric Service of Walter Levy, M.D., and the Surgical Service of Benjamin Sherwin, M.D., the Jewish Memorial Hospital.

home entirely well. After this episode, he was examined at regular monthly intervals. His appetite was good, and growth and development were excellent. The only abnormal findings consisted of an enlarged liver that was palpable 2 cm. below the costal margin, and a mild iron-deficiency anemia, which responded to orally administered ferrous sulfate.

One week before the present admission, during a routine physical examination, a large fusiform nontender mass was felt in the right upper quadrant of the abdomen. There had been no abnormal symptoms immediately before this finding; no loss of appetite, no vomiting, or fever. The stools had been occasionally loose, but generally were normal in color and consistency. At no time, even during the severe illness in the neonatal period, had jaundice been detected.

On admission to the Jewish Memorial Hospital, the following positive findings were revealed: enlarged and moderately inflamed tonsils; occasional wheezing rales at the base of both lungs; a firm, smooth, fusiform mass which occupied almost all of the right upper quadrant, was continuous with the liver, and extended to the umbilicus. The mass was movable in the longitudinal axis, not tender or pulsating. The spleen was not palpable. The lower pole of the right kidney could be felt, and did not move with the mass.

Laboratory Studies.—RBC 4,480,000; hemoglobin 11.6 gm. per 100 cc.; WBC 9,800, with polymorphonuclear leucocytes 28%, lymphocytes 70%, monocytes 2%, ESR 12 mm. in one hour (Westergren); platelets 403,200; reticulocytes 1.2%; prothrombin time 15 minutes; blood sugar 55 mg. per 100 cc.; urea N 13 mg. per 100 cc.; thymol turbidity 0.7 unit; cephalin flocculation 2 +; alkaline phosphatase 19 K-A units; icteric index 5.5; total proteins 6.7 gm. per 100 cc.; albumin 3.8 gm. per 100 cc.; globulin 2.9 gm. per 100 cc.; A-G ratio 1.3; sodium 138 mEq.; potassium 4.6 mEq.; chlorides 114 mEq.; Mazzini test negative.

X-Ray Studies.—Heart and lungs normal; intravenous pyelogram normal; long bones normal except for slight tibial bowing. A flat plate of the abdomen revealed a soft tissue mass displacing the transverse colon downward and to the left. In order to determine whether the mass was intraperitoneal or retroperitoneal, a perirenal air insufflation was performed. This revealed a normal outline of both kidneys, and in the lateral view, the soft tissue mass was seen in the anterior third of the abdomen.

The preoperative diagnosis was hepatoma of the liver, although one of the attending surgeons remarked that if the patient were an adult, he would consider the possibility of hydrops of the gall bladder.

At operation, a massively enlarged gall bladder was found, with a capacity of at least 4 oz., (118 ml.). The liver appeared normal. The lower half of the gall bladder was bound by old adhesions to the omentum and duodenum. The wall was thickened and showed evidence of inflammatory changes. No calculi were palpable, and there was no emptying on pressure. The gall bladder contained turbid brown fluid. The common duct was normal. The cystic duct in its proximal two-thirds was as large as the common duct. Bile aspirated from the common duct was normal in appearance. The appendix was normal. A cholecystectomy was performed. The infant had an uneventful postoperative course and was discharged 10 days later. At the present time he is in excellent health.

Pathologist's Report.—The gall bladder was 9 by 3.5 cm.; the walls were thickened, and no calculi were present. There was a ring of fibrous tissue in the cystic duct which completely occluded the lumen. Findings on culture of the fluid were negative. Microscopic sections revealed a fibrotic wall and a flattened mucosa consisting of a single layer of columnar cells.

The diagnosis was dilated gall bladder with subacute inflammation and obstruction of the cystic duct.

COMMENT

Hydrops of the gall bladder may be due to transient and mild infectious cholecystitis, usually with a calculus obstructing the cystic duct. Baumgartner [2] studied 4,575 gall bladders at Mayo Clinic; he found 158 cases of hydrops, and stones were absent in only 6. Occasionally the stone may pass into the common duct and intestinal tract and not be found at operation. With complete obstruction the bile in the

gall bladder is slowly absorbed and replaced by a serous transudate from the inflamed bladder wall.[4] A characteristic pear-shaped tumor develops, and may attain considerable size without appreciable symptoms.

Although infection has been considered the chief cause of cholecystitis in children, it is less likely to play a prominent role in the future, largely due to the extensive use of antibiotic therapy. Bonta and Lovingood [5] have shown that the incidence of cholecystitis in the past decade is lower than the the preceding one. On the other hand, it is conceivable that other factors may contribute to a higher incidence of biliary tract disease. The survival rate of newborn infants with severe reactions from Rh and ABO incompatibilities has risen greatly, with the employment of early replacement transfusions. After this procedure, a number of infants with erythroblastosis developed an inspissated bile syndrome. Hsia [6] reported a series of 25 such cases associated with protracted jaundice and liver dysfunction. Although many of them ultimately developed cirrhosis of the liver, they also showed evidence of inflammation of the biliary system. In other instances of the inspissated bile syndrome it was impossible to differentiate the original cause from cholangitis.

In hemolytic disease other than in the newborn, involvement of the gall bladder is manifested by the presence of pigment stones. Gross [7] pointed out that the presence of biliary calculi in early life is almost always an indication of previous hemolytic crises. The concentration of bile pigments in the circulating blood may reach extremely high levels, and concentration in the gall bladder enhances the possibility of stone formation. The tendency to use repeated transfusions for thalassemia and sickle-cell anemia may give rise not only to hemosiderosis, but also involve the biliary tract as well.

The pathogenesis of the hydrops in this infant arouses interesting speculation. Obviously, the immediate cause was the fibrous obstruction in the cystic duct. There is no evidence to indicate that this was congenital in origin, although most cases of gall bladder disease in this age period are associated with a congenital anomaly. It is also difficult to determine when he developed the cholecystitis. All of the recently reported cases, including those of Bonta and Lovingood,[5] Lowenburg and Mitchell,[8] Kahle and Jackson,[9] and Lee and Englender,[10] were associated with acute symptoms of fever, abdominal pain, and marked tenderness. None of these were observed in this infant preceding the discovery of the mass. A recent case of hydrops, reported by Narat [11] in a 4-year-old child, was associated with pain, abdominal tenderness, and vomiting.

Conceivably, the illness during the neonatal period, or the bronchopneumonia, contributed to the inflammation of the gall bladder, although there was no evidence of biliary tract disease during either of the illnesses. Liver damage in neonatal sepsis is not uncommon, but jaundice is usually present. The persistence of an enlarged liver, with slight increase in the cephalin flocculation tests, suggests that liver damage did occur at some time, even without jaundice, and cholecystitis could have developed even in the neonatal period.

The absence of symptoms from the hydrops is not unexpected. In adults, there may be only slight pain and a sensation of pressure as the gall bladder becomes distended. In an infant, such minor inconvenience may go unnoticed.

In establishing the diagnosis, it was necessary to determine whether the mass was intraperitoneal or retroperitoneal. The use of perirenal air insufflation was

of value in making this differentiation and helped to rule out such possibilities as Wilms's tumor, neuroblastoma, and retroperitoneal sarcoma. Once the mass was established as intraperitoneal, it had to be distinguished from carcinoma, hamartoma, or hemangioma of the liver.

One of the interesting aspects of this unusual case was the absence of interference with normal growth and development. Apparently a poorly functioning, or non-functioning, gall bladder with low-grade inflammation, need not impair an infant's digestion or general progress.

SUMMARY

An unusual case of cholecystitis with hydrops formation in a 14-month-old infant is presented.

The condition developed with complete absence of symptoms, in contrast to all other cases reported in children.

The possibility of cholecystitis arising during neonatal infection is discussed.

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Society Transactions

CHICAGO PEDIATRIC SOCIETY

Alfred S. Traisman, M.D., President

Regular Meeting, Oct. 20, 1953

The Role of the Pediatrician in a Local School Health Program. Dr. Maya S. Unna.

The pediatrician, owing to his special training in preventive medicine, growth and development, communicable disease control, and preventive psychiatry and his special interest in the child as he grows up in his family and community, will be in a position to integrate his knowledge with the expressed needs of the educators in the school administration towards the maintenance of health in the school population.

Emphasis is given to the functioning of the physician within his local community, where he can bring into play the year-long confidence he has enjoyed in caring for the sick and thus help in motivating the public school leaders and other physicians in the community toward a school health program of high standards.

School health program may be defined in various ways due to the specific needs and available resources prevalent in the particular community.

The importance of size and scope of program, i. e., school population, number of schools, and number of nurses per school child, as well as social factors in the community, such as educational standards, income level, ethnic background, and communication facilities, are mentioned. Advantages of a well-functioning medical society, closeness to medical educational centers, and availability of funds for specialized programs are stressed.

The four functions of the school health program, health appraisal, screening and case finding, follow-up work, and health education, should be closely related to the practicing physician's work in the school area. Again the pediatrician may play a strategic role in coordinating the desired services.

Particular importance is placed on the fact that parents, school people, and physicians consider this "their" school health program.

Elaboration and exemplification of various possibilities in different communities are given.

Organizational charts of various school systems and their integration of health services are presented. The special place which a so-called mental health program in various school systems may be occupying will depend on a variety of factors and is shown in flow charts.

The Lyons Township School Health Program is given as an example. Here local physicians, on the initiative of the pediatricians, have taken on various committee chairmanships and work in close relation with school nurses and administrators.

Methods of evaluation of existing school health services are presented with references to the literature and to a statistical approach. The difficulties in evaluating a specific program, i. e., Lyons Township School Health Program, are discussed candidly. Here again, the crucial role of the pediatrician in relation to quality of school health activities is stressed.

The physician working with a school health program must be able to create and maintain and correlate the following factors: training and awareness of children's needs; availability and communication, improved with and within the school, home, and community; knowledge of the school and community, and collaboration between persons, professions, and agencies.

Lyons Township School Health Council consists of the schools, parochial, elementary, and high; the participating members, administrators, nurses, teachers and counsellors, family doctors, PTA, clergy, dentists, specialists, janitors and children; committees, first aid policies, standing orders, forms and records, communicable disease (immunization and readmission policies), mental health, handicapped children, and health education.

DISCUSSION

DR. NORMAN T. WELFORD: I should like to make one or two remarks about the Lyons Township program. The School Health Committee meets frequently as a committee, but in addition the pediatrician has a very friendly relationship between himself and the school nurse, the teachers, the coaches, and others, and in all the small discussions (groups of 10 or 12 people), he tries to make them all feel that they are free to call upon him at any time for information which may be of help to them in the care of the children in school. The pediatrician, in turn, enjoys a reciprocal relationship whereby he feels free to call upon the teachers in the schools, or the nurses, at any time when there are matters pertaining to the child's care. It is not unusual for nurses in the community to call an impromptu meeting with the pediatrician for the purpose of discussing problems which they feel should not wait over until the regular committee meeting. The informality of these meetings is what makes them successful, leading to success in our over-all school health program.

In the Lyons organization, participating membership includes the athletic coaches. These coaches sit in on the general meetings and are given a feeling of responsibility beyond that of just producing good athletic teams. One other matter, which I have long thought very important in the success of any school health program, has to do with children who present various behavior problems. We should have a school setup whereby, when the child appears in the office for any problem relating to mental health, we can get all the information we need through the school health program to help in caring for the individual child.

Some 16 years ago, Dr. John Lovett Morse wrote a paper entitled "The Future of Pediatrics," in which he painted a very gloomy picture for the pediatricians in this country. He based his prediction upon the fact that at that time a strong trend towards socialization was beginning to gain momentum. At this time, he believed that the then powerful Children's Bureau, in Washington, would take over all activities pertaining to child care, including the school health programs. With the passage of time, I think it has been proved that the contrary has been true, and I think the establishment of the School Health Programs with support of the entire community is one case in point.

Again, it is interesting to look back some 22 years ago, when Dr. Joseph Brennemann published his paper "The Menace of Psychiatry." Actually, Dr. Brennemann was not opposed to psychiatry. He simply objected when these matters got out of the hands of those trained in pediatrics and in child training. He was very much in favor of the pediatric psychiatrist but felt many of the divisions of child care, including the school health programs, might easily fall into the wrong hands. Dr. Brennemann put out a pamphlet "The Health Crusade for Schools." It is interesting to compare the school health program of 22 years ago with that of today. In the health crusade, a system of training children in good health habits was popularized, and many children were reached through this movement. One example was a health chart, given to the children, on which each child recorded his own behavior on 10 points: Did he wash his hands, his face, his neck and ears? Was his posture good? Did he polish his shoes? How often did he brush his teeth? Did he take his rubbers and coat off when indoors, even when not at school? The health crusade sought to make good health habits attractive.

It seems most appropriate that this discussion should take place at this particular time. Only two weeks ago the annual meeting of the School Health Committee of our national organization, The American Academy of Pediatrics, was held. Those of us who attended the meeting felt a deep sense of gratitude and admiration for the Pediatrician's Committee. On the platform were representatives of the various fields of school health, and each one who arose described some particular phase of the subject and gave something of real value in this whole field of school health. Back of this whole program and staunchly supported by each member of the committee, one could see the skillfully handled plan by the masterly hand of the Committee chairman of the National Committee, John L. Reichert. The policies outlined by the National Committee bear very close resemblance to the organizational setup which Dr. Unna has presented here tonight.

DR. JOHN L. REICHERT: Dr. Unna has opened up so much and has done it so well, on the whole question of the school health field, that I hardly know were to begin. She brought out the fact that they worked together in solving local problems, but the manner in which they solved their problems is very interesting, and I think we should all know more about it.

This discussion brings out one thing—that school health is not an isolated program. When the baby is born, however, the chief medical supervisor is the pediatrician, and I see no reason why he should surrender his position. Rather, he should work with those people who enter into the training of the child, those people who can keep him advised. They should work together, each contributing to the whole. The pediatrician must cooperate with the schools, the teacher must become his ally, the school nurse and the others all supplement the help which he can give in the care of the child. The pediatrician, if he is to take the leading role, must consider the schools and the family physician in carrying out this role. Particularly, I want to stress the importance of free lines of communication between the school and the pediatrician. You have probably all had the experience of catching a chorea early, when the teacher has said the child's handwriting was bad. In just 10 minutes, talking to the teacher and then to the mother, the pediatrician can often clarify the whole picture. They have done this beautifully in the Lyons program. Their program will probably help us in finding solutions to many of our local problems, since they have already met and solved many of these problems.

DR. MAYA S. UNNA: Thank you very much, not only for giving me the incentive to present this material but especially I want to thank Dr. Reichert for carrying out the thought that we are trying to integrate a little more educational cooperation within the medical profession. This is sometimes very hard to accomplish, and we should try to be very tactful about it—but even that is within our program.

A Chart to Record Growth and Performance. DR. E. ROBBINS KIMBALL.

A chart to record physical growth was constructed from the measurements of Stuart from Harvard for the first 5 years of life and from those of Meredith from the University of Iowa for the age period from 5 to 18 years. Height, weight, and, when necessary, the circumference of the head were recorded in percentiles. For example, a boy of one year of age weighed 25.4 lb. (11,520 gm.). It was observed that this figure at this age fell upon the 90th percentile, which means that he was heavier than 90% of the healthy children in America and lighter than 10%.

Also, various developmental tests were plotted against age. When the child performed, the appropriate test was checked off along the ordinate, and an appropriate remark as to the kind of performance was written in opposite age. When he did not perform, an arrow was marked opposite age accompanied by a descriptive remark regarding the nature of his technique of resistance. Overcautiousness and bold aimless aggression were the two types of techniques of resistance encountered. Three thousand infants and children were examined in this manner over a period of eight years. Of the first children in the family, 90% had some arrows beginning at 10 months and lasting through the third birthday. In most instances this was because the parents expected too much of them. The arrows in the younger siblings frequently coincided with mothers' illness or fatigue or inadequate use of the play pen, gates, and fences separating the toddlers from the mechanized adult world with its many noes. The 10% who had no arrows were all exceedingly well-adjusted children and parents. Two infant welfare nurses making repeated independent observations of these children and their parents at home agreed almost 100% with my observations at the welfare clinic. A 30-minute movie illustrated how the mother-and-child relationship was examined and recorded.

DISCUSSION

DR. E. ROBBINS KIMBALL: The principal difference between our use of the chart which I have presented, and those of Arnold Gesell, which we used in the beginning at the Evanston Infant Welfare, is that we consider the child not as a separate entity, as he did, but the relationship between the child and mother. We have also changed these tests to speed them up a bit. The movie which I have shown illustrates how the pediatrician carries out these tests while examining the baby, which gives him this mother-child relationship. This second point is, the effect which this has on the mother. The mother is given a better appreciation of just what she may expect from her own child.

DR. IWAN ROSENSTERN: I should like to congratulate Dr. Kimball on this presentation, in which he has brought out several things of very great importance.

First is this "mother-child relationship" concept. In this situation the examination is carried out under conditions which are not abnormal, and under these conditions the child's reactions

are apt to be normal. When tests are given to children without their mothers, conditions may be strange to the child, and he is easily frightened. For example, the child who has never seen a person wearing a mask may become frightened because it is new. It is much more difficult to get the child's normal reactions.

Second, notice how happy those children in the movie were. I can well remember, when the child was examined alone, the difficulties—the child always cried and was easily frightened, and there was great commotion. At the Infant Welfare Society everyone was very happy when these difficulties were eliminated.

Third, I think this picture shows a wonderfully successful method of examining the mental development of the young child.

I should like to ask several questions. I should like to know if there are some good tests for the first three months of life. I am interested because of the practice here in Chicago of placing babies earlier for adoption. Formerly, babies were 12 to 18 months of age when placed for adoption, and in some states there is a period of probation of six or nine months before the child can be adopted legally. Now babies are placed with families at 10 or 12 weeks of age, and sometimes even earlier. Tests are needed for these early ages.

I should like to make a few remarks about carrying out examinations at these early ages. I have seen doctors try to examine babies as young as 6 weeks. In attempting a mental test, the child does not know the answers. He is unlikely to know what is going on. He may be hungry and want his bottle—you cannot hold his attention—he wants his bottle, and that is all there is to it. The same is true of the baby who may be tired. He simply will not pay any attention to what is going on. Some babies will thrash about, and others will be so tired they will fall asleep. Perhaps in time the psychologists will work out tests which are more easily given to these very young babies, but the difficulties experienced in conducting them now make the tests of little use.

Dr. George Mohr: I was much impressed by this effort to gauge the mental development of very young children in terms which Dr. Kimball has made very explicit. He has impressed upon us that in the matter of growth and development it is not only a matter of observing the effect of physical bodily processes, but of observing what the child does. I think to give the mother a better appreciation of what she may expect from her own child is a real step forward. This is important not only in our professional practice, but particularly when it comes to dealing with children professionally, as in welfare stations. If these charts are used for large groups and large numbers of records are kept, they may be of use later on. I think the emphasis on this approach is very conclusive, certainly from the standpoint of the pediatrician who is also interested in the psychological development of children.

Dr. E. Robbins Kimball: In closing, I wish to thank Dr. Rosenstern and Dr. Mohr for their kind remarks. I only wish I could answer Dr. Rosenstern's questions about tests for the very young babies, but I don't know how to do it. My object has not been the psychometric examination; that has been only a by-product of my efforts. We have been more interested in the emotional climate of the child, and when I started out I was very much inclined to favor environment. Now my interest is more in how the brain is built and whether or not it has been injured. Of course I cannot add anything more to the adoption problem. I don't know how the tests can be done.

Abstracts from Current Literature

Metabolism; Infant Feeding; Milk and Other Foods

RELATION OF SERUM CHOLINESTERASE TO NUTRITIONAL STATUS OF ADOLESCENTS. JACK P. SAUNDERS, HAROLD R. SANDSTEAD, ROY E. BUTLER, and OLAF MICKELSEN, J. Nutrition **47**:191 (June) 1952.

The relation between serum cholinesterase and nutritional status as measured by the parameters used in this study is such that the serum enzyme level contributes nothing toward the nutritional appraisal of people in a condition similar to that seen among Americans. In 119 children no useful relation was found between serum cholinesterase levels and hemoglobin, serum carotene, degree of underweight, physical signs indicative of malnutrition, or general appearance from a nutritional standpoint. One of the apparent drawbacks to the use of cholinesterase levels as a measure of any physiological function is the great individual variation. Recent surveys have revealed only a small percentage of the people in this country to be severely malnourished. Thus there is a good chance for argument as to whether the underweight children studied in Washington are comparable to the previous persons studied by McCance and co-workers and Hutchinson and co-workers in Wuppertal, Germany, in 1946.

FREDEEN, Kansas City, Mo.

THE EFFECT OF HEAT ON THE NUTRITIVE VALUE OF MILK PROTEINS AS INFLUENCED BY WATER AND FAT. LAWRENCE J. SCHROEDER, MICHAEL LACOBELLIS, HELEN LEES, and ARTHUR H. SMITH, J. Nutrition **50**:351 (July) 1953.

The data in this paper, secured both by the nitrogen-balance method on intact animals and by in-vitro-digestion experiments with crystalline enzymes, show that the diminution in nutritive value suffered by the contained proteins when dried skim milk is autoclaved is prevented by prior reconstitution with water to protein levels as high as 24.5%. This present study demonstrates that the presence of water, even in minimum amounts, exerts a retarding influence upon the interaction of carbohydrate and protein regularly brought about by heat in the dry state. The data further show that the presence of milk fat has a minimum effect upon the apparent interaction of proteins and reducing sugars.

FREDEEN, Kansas City, Mo.

STUDIES ON THE FUNCTION AND METABOLISM OF COPPER. MAXWELL M. WINTROBE, GEORGE E. CARTWRIGHT, and CLARK J. GUBLER, J. Nutrition **50**:395 (Aug.) 1953.

Wintrobe, Cartwright, and Gubler found that in copper-deficient swine fed ample amounts of iron the total body content of iron, as measured by chemical assay of the tissues or by measurement of radioactive iron, is low, as compared with normal. Copper therapy without the simultaneous administration of iron in such animals is ineffective. In swine made deficient in both copper and iron, no increase in plasma iron follows iron therapy, but an increase takes place promptly when copper is given as well. Copper apparently favors iron absorption from the gastrointestinal tract. Copper is also concerned in the mobilization of iron from the tissues. Analysis of the iron content of copper-deficient animals reveals that the chief depletion of total body iron is in the hemoglobin compartment. This suggests that movement of iron from the tissues to the plasma is decreased. Thus in the copper-deficient swine the administration of copper is followed by a very sharp rise in the plasma iron content. That impaired utilization of iron for hemoglobin synthesis is another factor in the disturbed iron metabolism of copper deficiency is indicated by the fact that the intravenous or intraperitoneal administration of iron fails to relieve that anemia in copper-deficient animals. Studies with intravenously administered radioactive iron reveal that the uptake of iron for hemoglobin synthesis is poor in copper-deficient swine.

FREDEEN, Kansas City, Mo.

ABSTRACTS FROM CURRENT LITERATURE

PHYSIOLOGICAL PRINCIPLES IN THE MANAGEMENT OF FLUID AND ELECTROLYTE PROBLEMS IN INFANCY AND CHILDHOOD. W. B. MACDONALD, M. J. Australia **2**:197 (Aug. 8) 1953.

Fluid and electrolyte balance in young children is discussed briefly. Regulatory mechanisms are described, as well as specific effects of the various electrolytes, and principles of treatment are outlined.

McGUIGAN, Evanston, Ill.

FLUID AND ELECTROLYTE PROBLEMS IN INFANTS AND CHILDREN: INTESTINAL OBSTRUCTION. E. S. STUCKEY, M. J. Australia **2**:205 (Aug. 8) 1953.

Patients with high intestinal obstruction are usually suffering from a mixed form of dehydration due to abnormal loss of intestinal secretion by vomiting or aspiration and failure to take maintenance amounts of normal fluids. Intravenous feeding is required until these factors are overcome.

Treatment should not wait for laboratory tests. Tests should be used instead as measures of progress in treatment. Replacement of fluids is the first requirement. After this, maintenance fluids are given in amounts calculated to meet daily body requirements. Potassium as well as sodium should be included. After the second day, protein, vitamins B and C and, if necessary, blood should be given.

McGUIGAN, Evanston, Ill.

SUBSTANCES DERIVED FROM ETHYL BISCOUMACETATE (TROMEXAN ETHYL ACETATE) IN MOTHER'S MILK AND THEIR PARADOXICAL ACTIONS ON PROTHROMBIN. GOSTOF, HOMOLKA, and ZELENKA, Schweiz. med. Wchnschr. **82**:764 (July 26) 1952.

Using the method of Kaulla and Pulver, the authors determined the concentration of ethyl biscoumacetate (Tromexan Ethyl Acetate) and derivatives of ethyl biscoumacetate in blood and milk of mothers treated with ethyl biscoumacetate, as well as in the blood of nurslings. When ethyl biscoumacetate is added to human milk, its consumption by the nursling produces a lowering of the prothrombin of its blood; whereas milk from a mother having received ethyl biscoumacetate, produces an increase of its prothrombin. On a standard dosage of ethyl biscoumacetate, 3 to 6 mg. per 100 cc. is found in the milk, besides its derivatives. Infants receiving such milk present hemorrhages more frequently, compared with the average frequency of hemolytic disease of the newborn. The lowered capillary resistance caused by ethyl biscoumacetate only results in hemorrhages in regions where the blood vessels have been injured previously, as in the umbilical region or the head (cephal hematoma), without reference to prothrombin concentration. The substance (or substances?) has not been identified.

AMBERG, Rochester, Minn.

PHYSIOLOGY OF AMINO ACID METABOLISM AND ITS SIGNIFICANCE FOR THERAPY. H. BERGER, Schweiz. med. Wchnschr. **83**:761 (Aug. 15) 1953.

Berger reports that besides paper chromatography, the determination of the total amino acids by the method of Antener proved advantageous. It is a micromethod based on the colorimetric determination of amino acid nitrogen of Folin, requiring but 0.1 cc. of blood. Amino acids were determined in the blood of normal infants and in infants with cystic fibrosis of the pancreas. While the increase of amino acids in the blood of the latter when fed casein was deficient, it was practically normal when amino acid mixtures were given. On simultaneous administration of glucose or levulose with amino acid mixture, the increase of amino acids in the blood in normal persons was much less than with the amino acid mixtures alone. Similar results were obtained on injection of epinephrine. Under different conditions, the response to repeated administration of amino acid mixture after a two-hour interval differs, inasmuch as while in some instances no further increase occurred in the blood, in others a renewed marked increase was noted. Amino aciduria was also studied under various conditions. In some cases of lipoid nephrosis, a prolonged administration of amino acid mixture in sufficient dosage appeared to be beneficial.

AMBERG, Rochester, Minn.

DISORDERS OF CARBOHYDRATE METABOLISM IN DYSTROPHIC INFANTS. C. SALAZAR DE SOUSA, Minerva pediat. **4**:156 (March 15) 1952.

The author reports that 25% of dystrophic infants have a normal blood-sugar curve on a glucose tolerance test, 43% have curves of the diabetic type, and 15% have curves indicating increased tolerance, or hyperinsulinism. Thus, dystrophic infants should not all be treated in the same way. Many of the cases with a low tolerance may be the result of a fatty liver. Adrenal cortex deficiency may be a responsible factor in the hyperinsulinism cases.

HIGGINS, Boston.

THE SERO-PROTEINS IN THE NORMAL INFANT WITH SPECIAL REFERENCE TO THE GAMMA GLOBULINS. ORLANDO OLANDINI, A. SASS-KORTZAK, and J. H. EBBS, Rev. peruana pediat. **11**:99 (Oct.-Dec.) 1952.

Albumin, globulin, gamma globulin, and total-serum-protein values are presented in 140 normal infants from birth to 2 years of age, in 28 mothers at the time of childbirth, and in 13 healthy young adult women.

Values for most of the fractions in mothers and their newborn infants were found to be very close to each other except for globulins, which were higher in the mothers. Gamma globulin levels were found not to be significantly different.

In the first month of life important and striking changes were found in all fractions studied: (*a*) The albumin showed transient slight decrease in the first week, followed by reversal of this to the earlier level at the end of the first month of life. (*b*) The globulin values showed no change in the first week, followed by a sharp and marked decrease leveling off at about 1 month of age. (*c*) The gamma globulin showed a sharp decrease even in the first week. The decrease continued until one month of age. Absolute values at one month were about one-third of the values in the cord blood. (*d*) The total serum protein gradually decreased in the first month of life.

After the initial decrease, all fractions showed gradual increase up to 2 years of age. Adult values are closely approximated but not reached at 2 years of age. Normal values for total protein, albumin, globulin, and gamma globulin are presented from birth until 2 years of age.

FROM THE AUTHORS' SUMMARY.

THE COURSE OF HOSPITALIZED DYSTROPHIC INFANTS. JULIO MENEGHELLO, HERMANN NEIMEYER, JORGE ROSSELOT, FRANCISCO MARDONES, and OSCAR UNDURRAGA, Rev. chilena pediat. **23**:149 (April) 1952.

Infantile malnutrition is a serious problem in the authors' hospital population, due to its frequency and severity.

The authors reviewed 1,539 cases of infantile malnutrition hospitalized during the last eight years and noted many interesting facts. Most cases had a prolonged hospitalization (two-thirds of these stayed over one month at the hospital) as well as a high mortality rate (18.7%) principally caused by acute nutritional disturbances (toxicosis) during the warm summer months.

This study was based on a study of 1,113 chronically undernourished infants under one year of age, with a hospitalization period of four weeks or more, and arbitrarily limited to three months. The authors judged that during this period they could obtain a true picture of the course followed. Nevertheless, they insist that the exact picture of infantile malnutrition can only be obtained in a study that includes the initial as well as the recuperative stages of these disorders.

Keeping in mind that in the study of chronic infantile malnutrition the most important facts are seen as repercussions on the development and growth processes, the authors concentrated their study on the different phases of weight change. They made graphs of the weight changes of their cases and divided them into four groups as follows: (1) true and maintained progress (52%), (2) real progress with a prolonged recuperative period (22%), (3) stationary weight curve (23%), and (4) continuous decrease in weight (3%).

In the authors' experience neither age, hyposomia, nor the concomitance of infectious processes nor of acute nutritional disturbances influenced the development of the weight curves. Observation revealed the multiplicity and peculiar character of infections in the undernourished infant. The number of infections or of acute nutritional disturbances was less in those with a better weight curve. The authors' study revealed that the most frequent infectious processes

in 10 to 40% have a repercussion on the saline metabolism and lead to a condition of severe dehydration. They also noted a coexistence of different infections with great frequency (35 to 70%). The great frequency of infections in the undernourished infant and the sometimes not noticeable effect of the therapeutic measures probably are due to disorders of the immunity mechanisms. In 101 undernourished infants and in a group of healthy infants used as controls the authors noted that the initial values as well as those secondary to antigenic stimuli, to complement, and to the agglutinin capacity formation were less in the undernourished infants.

The authors concern themselves only with milk regimens. The greater relative importance of milk diets was noted in the infants under 3 months of age, with preferential use during the first six weeks of Eledón (human milk with powdered buttermilk) and, with less frequency, human milk or protein milk. The change from one of these modified milks to cow's milk was done earlier in the older infants.

During the first trimester an average of 130 to 160 Calories per kilogram of body weight per day was given, while in the fourth trimester between 80 and 110 calories was given. The authors established a relation between lower weight gains and fewer calories administered.

A tendency to give a larger energy supply in relation to the true weight of those infants with lower weights was noticeable. The supplies of carbohydrates were generally high, varying between 15 and 25 gm., although sometimes with values over 30 gm. per kilogram of body weight per day. The supply of fat was usually low (3 gm. per kilogram of body weight per day), low values that can be explained by the prolonged use of modified milks and also by the fact that only in exceptional cases were the caloric demands met with supplementary fat feedings. The protein supply was satisfactorily met by the so-called "curative milks," used over long periods. The younger infants proportionally received more protein than the larger infants (5 gm. per kilogram of body weight per day for the former, against 3.3 gm. per kilogram of body weight per day for the latter). There was no parallel between larger amounts of proteins received and satisfactory weight graphs.

To make possible a study of the protein adaptation of the undernourished children, nitrogen balance studies were undertaken in 22 patients in the recuperative phase. A diminished amount of intestinal absorption of nitrogen was found in the undernourished ($84 \pm 1.6\%$). The authors were able to demonstrate that nitrogen retention depends directly on the amount of nitrogen in the food and that within equal limits of nitrogen absorption the amounts retained are the same in normal and in undernourished infants. The increase of the caloric value of the diet was not necessarily followed by an increase of nitrogen retention. The authors also point out that there is no relation between the gain in weight of the malnourished infants and nitrogen retention, as they frequently observed excellent nitrogen retention values with no corresponding weight gains.

As complementary therapeutic measures they used antibiotics, plasma therapy, and vitamin supplements. To modify the anemia of the malnourished infant, vitamin B_{12} was given to 22 infants in a single dose of 10 gm. noting in three-fourths of the patients a reticulocyte response (over 10% in 11 cases and with values between 18 and 33% in 3 cases), an almost constant erythropoietic bone-marrow response, and with restoration of red cells in a majority of the patients. Fourteen patients received, over a period of six days, 15 gm. of vitamin B_{12} by intramuscular injection, thus obtaining an increase of the nitrogen retention that was more evident with a low basal protein supply.

The administration of testosterone in 18 patients left the authors with the impression that in approximately all cases there was a satisfactory clinical response. In two of these, nitrogen studies showed a greater nitrogen retention with high-protein diets.

The authors stress the difficulty of judging the effect of certain treatments in the cure of the malnourished infant, as the course of the malnutrition has many aspects, and in interpretation of the results one must always allow a margin for those cases that have a spontaneous evolution.

FROM THE AUTHORS' SUMMARY.

CYSTINE STORAGE DISEASE WITH AMINOACIDURIA AND DWARFISM (LIGNAC-FANCONI DISEASE): PART I. INTRODUCTION. H. BICKEL, W. C. SMALLWOOD, J. M. SMELLIE, H. S. BAAR, and E. M. HICKMANS, Acta pædiat. Supp. 90, 1953.

Fourteen children suffering from cystine storage diseases with aminoaciduria (Lignac-Fanconi disease) have been studied in the last three years, and the results are described in a

series of eight papers of which this first paper contains an short review of the literature, some general remarks on aminoaciduria, cystinuria, and cystine storage and a brief statement on some of the results obtained and conclusions reached. Publications by Lignac, Fanconi, Beumer and Wepler, and others, as well as our own observations, lead us to the conclusion that Lignac's disease (cystine storage disease) and Fanconi's syndrome of childhood (nephrotic glycosuric dwarfism) are one and the same disease. At the present time this disease cannot be identified with similar syndromes in which cystine storage has been excluded. The variability of nearly every symptom in Lignac-Fanconi disease is stressed. The most reliable diagnostic features besides dwarfing are cystine storage and aminoaciduria of a characteristic pattern. Cystine storage can be demonstrated in vivo by slit-lamp investigation in cornea and conjunctiva, as well as in bone marrow and lymph glands, and the cystine can be identified in biopsy material by microscopy, x-ray crystallography, and chromatography.

The aminoaciduria is accompanied by aminoacidemia, and the characteristic pattern in urine is best shown by paper chromatography. The differentiation from other forms of aminoaciduria, such as that of newborn infants and classic cystinuria, is discussed. Reasons are given why cystine storage and aminoaciduria are regarded as the result not of kidney dysfunction but of a prerenal disturbance of the whole aminoacid metabolism, probably situated within the reticulo-endothelial system.

FROM THE AUTHORS' SUMMARY.

CYSTINE STORAGE DISEASE WITH AMINOACIDURIA AND DWARFISM (LIGNAC-FANCONI DISEASE): PART II. THE GENETICS OF LIGNAC-FANCONI DISEASE. H. BICKEL and H. HARRIS, Acta pædiat. Supp. 90, p. 22, 1953.

Lignac-Fanconi disease has often been described in siblings but never in different generations. Our findings in the families of eight patients, including chromatographic studies of 138 urine specimens, confirm these observations. Of a total of 19 siblings, 4 were probably and 1 certainly affected. No other relatives suffered from the disease. Consanguinity was found in one family; its incidence also seems to be raised in the literature. The data suggest that Lignac-Fanconi disease is genetically determined and of simple Mendelian recessive character, but that it is not genetically related to classical cystinuria or to the so-called Fanconi syndrome in adults. The frequency of Lignac-Fanconi disease in the general population is estimated to be roughly 1 in 40,000, with a gene frequency of 1 in 200. The genetical prognosis is believed to be one in four for any subsequent child of parents who already have one sick child. Corresponding figures are given for cousins of the patient and for children of the patient's siblings.

FROM THE AUTHORS' SUMMARY.

CYSTINE STORAGE DISEASE WITH AMINOACIDURIA AND DWARFISM (LIGNAC-FANCONI DISEASE): III. CLINICAL DESCRIPTION, FACTUAL ANALYSIS, PROGNOSIS AND TREATMENT OF LIGNAC-FANCONI DISEASE. H. BICKEL, W. C. SMALLWOOD, J. M. SMELLIE, and E. M. HICKMANS, Acta pædiat. Supp. 90, p. 27, 1953.

Clinical manifestations of Lignac-Fanconi disease are dwarfing and wasting, rickets and osteoporosis, pyrexia, eye changes (sometimes with photophobia), vomiting, polydipsia and polyuria, dehydration, acidosis, sometimes tetany, states of profound collapse, and even sudden death. Acute and chronic forms of the disorder are described. Laboratory investigations reveal aminoaciduria, glycosuria, and sometimes albuminuria and ketonuria. In the plasma there is aminoacidemia, evidence of acidosis, hypopotassemia, and uremia, which may be renal or intrarenal.

In a short factual analysis the phosphorus-calcium, protein, electrolyte, and sugar metabolism as well as liver and kidney functions are discussed. A special section deals with ECG changes, and electrophoretic investigations are described in an addendum. The diagnosis "Lignac-Fanconi disease" should be suspected in all stunted children whose dwarfing is not obviously the result of other causes. Rickets, sometimes with severe deformity, evidence of kidney dysfunction, and glycosuria are further clinical features, while the discovery of cystine storage and the demonstration of aminoaciduria with a characteristic amino acid pattern provide final proof of Lignac-Fanconi disease. Differential diagnosis from renal rickets, resistant rickets, celiac disease, renal acidosis, galactosemia, and glycogen-storage disease may sometimes be

difficult. Treatment of the rickets with massive vitamin D doses, of the acidosis with Albright's solution, and of the hypopotassemia with potassium salts has proved encouraging; acidotic and hypopotassemic crises have ceased, the children have gained weight and grown slowly, their rickets is cured, and they are livelier. Perhaps the most striking effect of prolonged alkalinization is the gradual disappearance of aminoaciduria. The case records are given in an addendum.

FROM THE AUTHORS' SUMMARY.

CYSTINE STORAGE DISEASE WITH AMINOACIDURIA AND DWARFISM (LIGNAC-FANCONI DISEASE): IV. THE RADIOLOGY OF LIGNAC-FANCONI DISEASE. R. ASTLEY, C. G. TEALL, and H. BICKEL, Acta pædiat. Supp. 90, p. 98, 1953.

The radiological findings in seven children with Lignac-Fanconi disease are described and compared with those in the literature. Bone changes may be absent. When present, they are those of simple rickets, or, in the more chronic cases, of long-standing late rickets. The appearances are nonspecific and not distinguishable from those of avitaminosis D or from "resistant" rickets. These observations agree with theoretical conceptions because the bone changes, contrary to previous belief, probably originate in a failure of intestinal absorption of phosphorus and calcium.

FROM THE AUTHORS' SUMMARY.

Vitamins; Avitaminoses

BLOOD AND BONE MARROW STUDY OF VITAMIN-DEFICIENT RATS. KENNETH WERTMAN, ROBERT ROTUNDO, and ROBERT YEE, J. Nutrition **50**:479 (Aug.) 1953.

Wertman and co-workers concluded from their data that the vitamin deficiencies and inanition resulted in a marked leukopenia, and no significant effect was observed on the total erythrocyte count in the peripheral blood of the groups of rats studied. A change in the differential blood cell count of peripheral blood was noted in the thiamine-deficient, totally vitamin B complex-deficient, and inanition groups. The number of polymorphonuclear neutrophiles per cubic millimeter was not appreciably altered. This is accounted for by a percentage increase of these cells in the deficient animals. A marked reduction of lymphocytes per cubic millimeter in number and percentage was noted.

The bone marrow of rats with thiamine deficiency and total vitamin B complex deficiency showed a marked relative granulocytosis, with a corresponding increase in the younger myeloid cells when compared with the marrow of the ad libitum control animals. The bone marrow of the vitamin-deficient and the inanition control rats demonstrated a relative lymphocytopenia and slight increase in granulocytes. The changes in the number of nucleated red blood cells in the bone marrow were almost as great as those which occurred with respect to the total granulocytes. A lower median value for nucleated red blood cells in the thiamine-deficient groups was obtained.

FREDEEN, Kansas City, Mo.

THE UTILIZATION OF CAROTENE. WILLIAM H. JAMES and IBRAHIM M. ELGINDI, J. Nutrition **51**:97 (Sept.) 1953.

In the present experiments, James and Elgindi found that vitamin A was stored in the liver of each rat and suggested that the animals converted carotene to vitamin A in amounts sufficient to satisfy all physiological needs. The minimum value of the intake of vitamin A necessary for these needs—that is, the daily amount of vitamin A adequate for the good growth and general well-being of the rat but permitting little or no storage—has been reported by various investigators. That these physiological needs may vary, depending upon the type of protein in the diet, is suggested by the finding of significantly greater amounts of unaccounted for carotene associated with the zein-casein ration. The antithetical patterns of the data suggest that vitamin A is consumed in a liver process which transforms moieties from the ingested protein to other proteins or amino acids which the body tissues can utilize.

FREDEEN, Kansas City, Mo.

ROLE OF VITAMINS IN ANTIBODY PRODUCTION. A. E. AXELROD, Metabolism **2**:1 (Jan.) 1953.

The author summarizes his own work to date on the relationship between vitamin deficiency and antibody production in rats. Serum antibody production was measured after intraperi-

toneal injection of Group O, Rh-positive human red blood cells. Deficiency in pantothenic acid, pyridoxine, riboflavin, and folic acid resulted in a marked depression in the ability to produce antibody.

KAPLAN, Cincinnati.

A CASE OF CONGENITAL RICKETS. RAYMOND J. TERRAFRANCA and ALLAN ZELLIS, Radiology **60**:192 (Feb.) 1953.

A newborn infant was shown to have the advanced changes of rickets on roentgenograms of the bones made when 2 days of age. The mother, a 16-year-old Negro girl, had prenatal bleeding, and at delivery the placenta showed evidence of 10% premature detachment. The fact considered most strongly as the cause of rickets in this case was a rachitogenic diet self-imposed by the mother.

ANSPACH, Riverside, Ill.

VITAMIN D RESISTANT RICKETS. DOUGLAS GALBRAITH, M. J. Australia **2**:208 (Aug. 8) 1953.

Rickets resistant to vitamin D may be due to idiopathic resistance to vitamin D or to several kinds of renal disease. Idiopathic resistance is rare, and probably most resistant rickets is due to various renal disorders.

Glomerular rickets is due to failure of the glomeruli to excrete phosphates so that there is an increase in blood phosphates. In failure of tubular resorption, phosphates are not reabsorbed, and there is a consequent loss of blood phosphate.

Treatment depends on correction of the biochemical defect. Where acidosis is not present, improvement may be obtained by large doses of vitamin D. If acidosis is present, alkali therapy is essential. Citrate therapy is useful in promoting a positive calcium balance.

McGUIGAN, Evanston, Ill.

URINARY EXCRETION OF RIBOFLAVIN BY HEALTHY INFANTS AND BY INFANTS WITH RIBOFLAVIN DEFICIENCY. G. RUSSO, Minerva pediat. **4**:753 (Sept. 15) 1952.

Observations were made on 31 infants under 2 years of age; 18 were in normal health, and 13 had clinical signs of riboflavin deficiency. Balance tests were made, determining the daily intake and the urinary output of riboflavin under normal conditions and also after intramuscular injections of 2 mg. riboflavin. The mean difference between the food intake and the urinary excretion of riboflavin per day was 585 γ in the normal infants and varied from 50 to 93% of that figure in the children with avitaminosis. When riboflavin was injected, increased elimination of the vitamin was apparent for 48 hours. Most of the infants with avitaminosis retained a higher percentage of the injected riboflavin than did the normal children, although others seemed to have been unable to utilize it.

HIGGINS, Boston.

RICKETS AND CITRIC ACID. S. NORDIO, Minerva pediat. **5**:189 (March 31) 1953.

The giving of 1.5 gm. of citric acid daily to each of 18 rachitic children led to an increase in the blood calcium in 12 cases and a decrease in 6 cases and to an increase in blood phosphorus in 9 cases and a decrease in 9 cases. In only four cases was there an increase in both blood calcium and blood phosphorus, and in none was there a decrease in both blood calcium and blood phosphorus. No clinical improvement in the rickets was noted in these children. The administration of citric acid seemed to accelerate the action of vitamin D in curing the rickets in children.

HIGGINS, Boston.

EFFECT OF COCARBOXYLASE ON THE GLUCOSE TOLERANCE CURVE. V. BAFFI and L. SCIEUZO, Pediatria **60**:310 (May-June) 1952.

Observations on 10 children showed that, when 100 mg. of cocarboxylase was administered, the glucose-tolerance curve showed a definitely lower blood sugar level. This finding is explained on the grounds that cocarboxylase hastened the synthesis of glycogen.

HIGGINS, Boston.

TWENTY-FIVE YEARS OF VITAMIN D THERAPY. M. SCHMIDTMANN, Deutsche med. Wchnschr. **78**:1300 (Sept. 18) 1953.

In a pathological institute, 240 children of various ages were examined, with particular attention to the ascending arch of the aorta and the coronary arteries at their aortic origin. Changes were seen most frequently in children 3 years of age after previous treatment with vitamin D_3 (Vigantol). Yellow foci up to fingernail size were located in the middle of the ascending aorta with swelling, splintering of the elastic fibers, and deposition of calcium. Such lesions did not occur in older children. Lesions of the coronary arteries were only found in one infant, dying at the age of 6 weeks. The child had received vitamin D_3. On postmortem examination, besides an isthmus stenosis, an isolated coronary calcification was found with scar formation in the heart muscle and a fresh extensive disorder of circulation. Vitamin D hypervitaminosis is discussed.

AMBERG, Rochester, Minn.

Hygiene; Growth and Nutrition; Public Health

SCHOOL HEALTH IN ILLINOIS. GEORGE L. DRENNAN, Illinois M. J. **103**:227 (April) 1953.

In Illinois, with its existing and potential resources, it should be possible to achieve the goal of providing adequate total health supervision for all children in the state. Among the indications of increased interest in school health are the development of school health councils; the formation of school health committees in medical societies; the institution of health courses in teachers' colleges, and the holding of meetings, conferences, and institutions on school health. Drennan points out that the law requiring health examinations three times during school life has focused attention on these activities in Illinois.

Some of the problems involved are listed in the order of their priority: (*a*) the development and maintenance of a school environment that will promote mental and physical health, (*b*) carefully determined policies for prevention and control of communicable disease, (*c*) a carefully worked out program to cope with emergencies and to meet disaster situations, (*d*) a well-organized program of health instruction essential to laying the groundwork for healthful living throughout life, (*e*) procedures to single out children with conditions that may interfere with learning and a follow-through to assure their correction or adjustment, (*f*) a program of physical education adapted to individual needs to provide skills that will serve as an incentive to wholesome physical recreation throughout life.

The development of a school health program is a complex task. The efforts of parents, teachers, nurses, physicians, dentists, and many others will be needed. The integration of all these functions requires the closest cooperation and challenges all concerned.

BARBOUR, Peoria, Ill.

EVALUATION OF THE SKELETAL AGE METHOD OF ESTIMATING CHILDREN'S DEVELOPMENT: 1. SYSTEMATIC ERROR IN THE ASSESSMENT OF ROENTGENOGRAMS. DONALD MAINLAND, Pediatrics **12**:114 (Aug.) 1953.

Because of the increasing use of skeletal maturation in the study of children's development and health, thorough exploration of the systematic and variable errors of skeletal age assessment is desirable. The systematic error of one observer (RBM) has been studied by comparing her assessments of hand roentgenograms reproduced in Macy's "Nutrition and Chemical Growth in Childhood," with the published assessments of the same roentgenograms by experts using the same atlases—Todd and co-workers using Todd's atlas and Pyle using the Greulich-Pyle atlas.

RBM's assessments, including duplicate readings on each roentgenogram, were all independent of each other, i. e., made without knowledge of chronologic age, of other assessments of the same roentgenogram, of other roentgenograms from the same child, or of any other information about the child except sex.

RBM tended to estimate the skeletal ages lower than did the experts, and this tendency was greater in the Greulich-Pyle comparison than in the Todd comparison. Her systematic error varied significantly between children and between roentgenograms of the same child. It is suggested that these variations may have arisen from the experts' assessments not being strictly independent.

Even if other observers had as large and as variable a systematic error as RBM, the skeletal assessment method would probably be sufficiently reliable in the comparison of average skeletal ages of groups of children, but it would be of doubtful value in the assessment of a single roentgenogram or of a child's progress.

Comparison of the expert assessments with each other showed that the change of the atlas (from Todd to Greulich-Pyle) has altered greatly some of the estimates of skeletal ages in the Macy roentgenograms and even expert assessment has not yet reached a desirable degree of stability.

The requirements in the preparation of a series of test roentgenograms by an expert are outlined. An experiment is described which the reader can conduct on the Macy roentgenograms, and an appeal is issued for the contribution of the data from such experiments to a survey of errors in skeletal assessment.

FROM THE AUTHOR'S SUMMARY.

GROWTH IN HEAD WIDTH DURING THE FIRST TWELVE YEARS OF LIFE. HOWARD V. MEREDITH, Pediatrics **12**:411 (Oct.) 1953.

This paper brings together the research findings on biparietal diameter from more than 50 investigations. It constitutes a synthesis of present knowledge pertaining to the head breadth of physically normal North American infants and children.

There are sections on the following topics: methodologic considerations, means for head width, variability in head width, findings from longitudinal data, and the relation of head width to other variables. Included in the section on variability is a table of norms and comments on its clinical use.

Representative generalizations are as follows:

1. The average North American white child attains 30% of adult head width by the middle of prenatal life, 60% by birth, 80% by 6 postnatal months, 90% by 3 years, and 95% by 9 years.

2. Throughout the period from birth to 12 years, the two sexes differ systematically: Head width distributions for North American white girls have slightly lower means and smaller standard deviations than comparable distributions for boys.

3. At one year of age, the limits of normal variation in head width are 11.4 cm. and 14.8 cm. for North American white boys, 11.1 cm. and 14.3 cm. for North American white girls. The normal limits at 10 years of age are 12.9 cm. and 16.3 cm. for boys, 12.7 cm. and 15.9 cm. for girls.

4. North American Negro school children have narrower heads than North American white school children, and North American Japanese school children have wider heads than North American white school children. The mean biparietal diameter of children of Mexican descent approximates that of American Negro children.

5. The association between width of head and length of head is low, of the order $r = 0.25$. A similarily low relationship exists between width of head and width of hips, but the relationship between width of head and width of face is appreciably higher.

FROM THE AUTHOR'S SUMMARY.

BIRTH WEIGHTS OF SOUTH AFRICAN BABIES. E. J. SALBER and E. S. BRADSHAW, South African M. J. **27**:317 (April 18) 1953.

Mean birth weights of South African babies vary with sex and race, as well as with economic status. Average weights of European and Negro babies are approximately the same as those in the United States.

McGUIGAN, Evanston, Ill.

EMBRYONIC GROWTH AND ITS DISTURBANCES. G. TÖNDURY, Schweiz. med. Wchnschr. **83**:175 (Feb. 21) 1953.

Special attention is paid to the development of the lens of the eye and the stage of development at which rubeola virus attacks the cells of the lens vesicle. More detailed information is given in other publications. The effect of the virus on the teeth is also discussed.

AMBERG, Rochester, Minn.

GROWTH FROM THE HISTOLOGICAL AND ULTRASTRUCTURAL POINT OF VIEW. C. A. BAUD, Schweiz. med. Wchnschr. **83**:185 (Feb. 21) 1953.

Illustrations of collagen microfibrils of the skin and myofibrils obtained by use of electron microscope are given, with a discussion of their growth from protofibrils.

AMBERG, Rochester, Minn.

ENDOCRINE GLANDS AND GROWTH. A. C. CROOKE, Schweiz. med. Wchnschr. **83**:194 (Feb. 21) 1953.

The author states that the growth curves of man and of various animals are compared and an analysis is made of the endocrine factors responsible for the differences between them. The article is written in English.

AMBERG, Rochester, Minn.

FLUORINE AND GENERAL HEALTH: STATE OF HEALTH OF A NATIVE POPULATION AND IMMIGRANTS IN THE VILLAGE OF SEMBRANCHER. V. DEMOLE and A. J. HELD, Schweiz. med. Wchnschr. **83**:362 (April 11) 1953.

Sembrancher is a village of about 750 inhabitants. Its water supply contains 1 to 1.4 mg. of fluorine per liter. The neighboring villages have water with much less or no fluorine. It is concluded that the use of the Sembrancher water, continued for several generations, has had no deleterious influence on its population. In children and adults the resistance to dental caries is remarkable. The few immigrants do not seem to have been affected by the consumption of this water. With food conditions considered normal for Switzerland, a concentration of 1 mg. of fluorine per liter of drinking water must be considered devoid of any toxic action on the tissues most sensitive to the action of fluorine.

AMBERG, Rochester, Minn.

TREATMENT OF THE JUVENILE DELINQUENT IN MONTEVIDEO, URUGUAY. ESTELLE F. KNOX, Bol. Inst. internac. am. protec. infancia **27**:320 (Sept.) 1953.

Uruguay treats the problem of delinquency mainly through prevention by taking care of children who are dependent or abandoned. However, when a delinquent act does occur, they try to reintegrate the child into society either through the help of his immediate family, a foster family, or, as a last resort, an institution.

It is apparent that the Uruguayan Children's Code is an example of the most modern liberal thinking in the treatment of juvenile delinquency. A cursory examination of the institutions set up to implement the code indicates that a sincere effort has been made to live up to the ideals which are contained in it. The care given to abandoned children; the efforts to reintegrate minors into the natural environment of the home, rather than attempting to intern them in institutions, and the work of reeducating maladjusted children point to clear thinking and a high sense of service to the community. Even the term delinquency is unacceptable to Uruguayan social scientists. They prefer to speak of "social error" (*falta social*), which in itself involves a step toward a rational analysis of the problem.

This paper was written to give a general impression of the treatment of juvenile delinquents in Montevideo to students who have no knowledge of Spanish; Spanish-speaking specialists can do better by consulting directly the references listed. The emphasis has been placed upon the activities of official government agencies, rather than upon the efforts of private or religious organizations. A more careful examination is required before final conclusions can be reached, for it appears possible that not all the techniques employed in the treatment of juvenile delinquents are equally advanced. It is also possible that the means given to carry out some of the programs envisaged by the code may not have been commensurate with the intricacy of the problems. It is intended that further study shall be undertaken on these matters within a short time so as to supplement this preliminary review, which is not intended to be definitive. On the whole, the Uruguayan approach to the problem of delinquency through its Children's Code is probably of the world's most advanced.

FROM THE AUTHOR'S SUMMARY.

INFANT MORTALITY IN THE CITY OF CASTELLO IN THE YEARS 1938 TO 1951. E. CENCI, Lattante **24**:258 (April) 1953.

The infant mortality statistics in Castello, a city on the Tiber River, are presented for the prewar, the war, and the postwar years. The infant mortality rate rose in the war years, but has fallen since the war ended. The fall has been mainly in infants with digestive or nutritional conditions, and in infants with infectious diseases, but not in premature infants or in infants with neonatal or congenital disorders.

HIGGINS, Boston.

STUDIES ON THE PHYSICAL DEVELOPMENT OF CHILDREN UNDER 2 YEARS OF AGE. C. CIRILLO and E. JANNONI, Lattante **23**:268 (May) 1952.

Two thousand children coming to the pediatric clinic in Naples and 620 from a nearby refugee camp for Slavic peoples were classified as to whether they were of normal or of abnormal development or whether they had a definite developmental pathology. All of the children were under 2 years of age.

The infants from Naples were all from the middle or poorer economic classes of the community; 27% were of normal development; 42% were of abnormal development, and 31% had a definitely pathological defect in their development. For the Slavic children, the figures were 16%, 33%, and 51%, respectively. Rickets was more frequently found among the Slavic than among the Naples group. The percentage of normally developed children was lower in the 1- to 2-year group than in the 0- to 1-year group.

HIGGINS, Boston.

THE BIRTH RATE AND THE DEATH RATE AMONG CHILDREN IN THE PROVINCE OF SIENA DURING THE YEARS 1946-1951. L. LANDUCCI, Lattante **24**:281 (May) 1953.

The birth rate in Siena has gradually dropped over six years from 15.9 to 12.2 per 1,000 population. In the same period the mortality among children under one year of age has fallen from 68 to 49 per 1,000 live births. In 1951, 92.8% of the deaths in children under 12 years of age were in infants under 1 year. Forty-seven per cent of the infant deaths were from congenital debility or malformations, 12% from respiratory infections, and 10% from gastrointestinal disturbances. Both the birth and death rates were lower in Siena than in Italy as a whole.

HIGGINS, Boston.

NEW SLANTS AS TO THE HEALTH OF CHILDREN. L. SPOLVERINI, Minerva pediat. **4**:168 (March 15) 1952.

The breathing of air which has been irradiated by ultraviolet rays is recommended as a means of improving nutrition and general physiological well-being and as a therapeutic adjunct in dystrophy, abnormal calcium and phosphorus metabolism, acute and subacute respiratory infections, and secondary anemia.

HIGGINS, Boston.

THE NATIONAL HEALTH SERVICE IN GREAT BRITAIN. GEORGE NEWNS, Maandschr. kindergeneesk. **20**:357 (Dec.) 1952.

A general review of the structure of the National Health Service is given. The hospitals which have been taken over by the State are grouped in 14 regions, controlled by a Regional Hospital Board. In England and Wales, 36 undergraduate and postgraduate teaching hospitals remain outside the regions and have a greater degree of autonomy. All of the hospitals, however, are under the control of the Minister of Health, who appoints the members of the hospital Boards of Governors. The hospitals are staffed by specialists who may be whole-time or part-time, the latter being allowed private practice. Payment varies with the amount of time spent on hospital work.

About 95% of general practitioners have joined the service. They are allowed up to a maximum of 4,000 patients and receive a capitation fee of approximately 17 shillings per patient per annum. Recently the maximum number of patients has been reduced to 3,500, and the capitation fee has increased. General practitioners can no longer buy a practice but are chosen

by a special local committee. Drugs have until recently been completely free, but a small charge is now made for each prescription. A complete free dental service is also provided, but, owing to the shortage of dentists, the patient has to wait a long time for treatment.

The National Health Service has benefited the patient but has thrown much extra work on the doctors, who have too many patients to look after. Recent changes may improve matters. Many smaller hospitals have been improved and adequately staffed. The teaching hospitals have been able to maintain their previously high standard. Unfortunately there has been a great increase in hospital running costs.

FROM THE AUTHOR'S SUMMARY.

Prematurity and Congenital Deformities

CARE OF THE PREMATURE INFANT IN MASSACHUSETTS. GERALD RICE, ETTA BLOOM, VLADO A. GETTING, and SALLIE SAUNDERS. New England J. Med. **248**:1090 (June 25) 1953.

Prematurity is recorded as the primary or contributory cause of death on approximately 50% of the death certificates of infants dying under one year of age in Massachusetts. In 1951, more than 1,000 infant deaths were recorded as being associated with prematurity.

The authors consider the efforts of the Commonwealth of Massachusetts to reduce the number of deaths deemed due to prematurity. The historical background is presented, along with an analysis of the problem, based on available statistics for 1951. The conclusions are colored by the fact that reporting by hospitals is often incomplete, and the authors make a plea for an effort by physician and hospital alike to advice the Department of Public Health of all births and deaths of premature infants.

WHEELOCK, Denver.

SOME EFFECTS OF EXOGENOUS THYROID OR THYROXIN UPON PREMATURE INFANTS. S. S. STEVENSON, P. WIRTH, R. BASTIANI, and T. S. DANOWSKI, Pediatrics **12**:263 (Sept.) 1953.

Forty-eight premature infants, whose condition seemed satisfactory at one week of age and whose weights approximated 1,500 gm., were selected for this study. Even-numbered infants in the series were given daily doses of desiccated thyroid or thyroxin for periods averaging three and one-half weeks; odd-numbered infants were given placebos of lactose according to the same schedule. The clinical progress of the infants was noted and weekly red blood cell counts and hemoglobin and serum protein-bound iodine levels were determined.

Daily doses of 1 or 2 grains of thyroid produced no significant effects upon clinical condition and progress or upon the protein-bound iodine level.

Daily doses of 3 grains of thyroid or 0.2 mg. of thyroxin did not affect the caloric and fluid intake, the gavage incidence, the amount of vomiting, the skin color, or the body temperature. Such dosage, however, decreased the weight gain, increased the pulse rate, and increased the incidence of diarrhea. A higher percentage of infants so treated required blood transfusions and did not fare so well clinically. The level of serum protein-bound iodine was elevated. The administration of thyroid or thyroxin to premature infants selected as noted above is therefore without observable benefit and is sometimes harmful. The effects of daily dosage with 0.2 mg. of thyroxin were at least as great as those with 3 grains of thyroid.

The mean protein-bound iodine level of 32 untreated infants was about 5.7 at an average age of nine days, and mean values for the control infants did not differ significantly from this figure during a subsequent five-week period. These levels do not suggest that the premature infant is deficient in circulating thyroxin.

Thyroid doses exceeding 2 grains per day are necessary to produce pharmacologic effects in premature infants and in euthyroid children and adults. This implies that the thyroid gland of the premature infant produces and releases thyroxin in amounts comparable to those of normal older human beings and approximating 2 grains of thyroid per 24 hours. Medication of the athyrotic cretin should be adjusted with this in mind.

When caloric intake is adjusted by the desires of the premature infant, he ingests an average of about 150 calories per kilogram of body weight per 24 hours. On such a regimen, his weight gain approximates that of his fetal colleagues of the same gestational age and averages more than 30 gm. per day.

AUTHORS' SUMMARY.

SYNDROME OF CONGENITAL HEMIHYPERTROPHY, SHORTNESS OF STATURE, AND ELEVATED URINARY GONADOTROPINS. H. K. SILVER, W. KIYASU, J. GEORGE, and W. C. DEAMER, Pediatrics **12**:368 (Oct.) 1953.

Two cases of a syndrome of hemihypertrophy, shortness of stature, and elevated levels of urinary gonadotropins are reported. One of the children was a male, the other a female.

The hemihypertrophy and shortness of stature had been present since birth and the elevated gonadotropins were found at 5½ and 6 years, respectively.

The possible relationship to other conditions in childhood, including those which also have increased gonadotropins, is discussed

FROM THE AUTHORS' SUMMARY.

PAYMENT FOR HOSPITAL CARE OF PREMATURE INFANTS. HELEN M. WALLACE, LEONA BAUMGARTNER, MARGARET A. LESTY, and HERBERT RICH, Pediatrics **12**:430 (Oct.) 1953.

This report describes the method developed by the New York City Department of Health to pay for the hospital care of prematurely born infants in six approved premature centers. It also discusses the results of this payment program. A total of $291,072.00 was paid for the care of 911 infants in a one-year period, of whom 38% were extramural infants. Family payment amounted to only 2.9% of the total funds expended. The average length of center stay was 26.6 days. Variations between centers were noted in the length of time it took the infants to reach their discharge weight of 2,500 gm. Thirteen per cent of the infants were kept in the centers after they reached 2,500 gm. in weight, approximately one-half of whom were kept there for nonmedical reasons. Some of the implications of the program for public health and hospital administrators, pediatricians, and social workers are discussed.

FROM THE AUTHORS' SUMMARY.

AMINO ACID EXCRETION AND KIDNEY FUNCTION IN PREMATURE INFANTS. J. STRODER, H. GRUNHOFER, and L. HEIM, Ann. pædiat. **180**:52 (Jan.) 1953.

The amino acid excretion in separate day and night portions has been ascertained in 12 premature babies during a 10-day experimental period. Day excretion exceeded that of the night. In spite of an increasing protein intake (up to 1.31 gm. per kilogram of body weight per 24 hours) and increased water excretion, it was found that the absolute amino acid excretion decreased during the 10-day period. The urinary amino acid values were higher at the beginning of the newborn period than at the end of the experimental period. The authors discuss the question of how far the concentrating power of the proximal part of the renal tubules may be responsible for the changing amino acid concentration. At present it cannot be decided whether the high amino acid concentration is brought about by the above-mentioned concentrating power or by a decreased resorption of amino acid in the tubules.

FROM THE AUTHORS' SUMMARY.

CHRONIC HYPERCALCEMIA COMBINED WITH OSTEOSCLEROSIS, HYPERAZOTEMIA, REDUCED GROWTH, AND CONGENITAL MALFORMATIONS. G. FANCONI and P. GIRARDET, Helvet. paediat. acta **7**:314 (Aug.) 1952.

Described at length are two cases, one from Zurich and one from London, of a peculiar, poorly understood syndrome having the following characteristics: (*a*) dwarfism and mental retardation, convergent strabismus; (*b*) persistent hypercalcemia; (*c*) moderate hyperphosphatemia (Zurich case) or a high normal serum phosphate level (London case); (*d*) evidence of renal disturbances, such as moderate albuminuria, persistent azotemia, lowered urea clearance, and, in the London case, hypertension; (*e*) definitely increased urinary excretion of calcium, less so of phosphates, the excretion of the latter clearly increased by an extract of the parathyroids (Parathormone [phosphaturia test]), in the Zurich case approximately 41% (normal 50 to 150%); (*f*) osteosclerosis, especially of the base of the skull but also affecting other bones, returning to normal with improvement of the general physical condition; (*g*) slight lowering of the alkali reserve; (*h*) slight elevation of the serum cholesterol; (*i*) normal serum levels of chloride and total base; (*j*) asymptomatic congenital heart malformations. The Zurich case shows, in addition, a premature closure of the cranial sutures, with resultant microcephaly. To

date, the disease seems to run a benign course; the two children are doing rather well; the disturbances of ossification and serum chemistry have improved. In the discussion, various possible explanations are dealt with; none of them are satisfactory. The disease picture conforms to neither a hypoparathyroidism nor a hyperparathyroidism, nor do any of the known primary nephropathies explain the syndrome. Neither the history nor the clinical course fits in with hypervitaminosis D. Primary diseases of bones produce no such disturbances of the serum chemistry and renal function.

FROM THE AUTHORS' SUMMARY.

THE TRIAD OF KARTAGENER: A CONTRIBUTION TO ITS HEREDITARY AND DEVELOPMENTAL BASIS. J. TORGERSEN, Schweiz. med. Wchnschr. **82**:764 (July 26) 1952.

The syndrome first described by Kartagener consists of situs inversus, bronchiectasis, nasal polyps, or a chronic hyperplastic rhinitis. Two sisters, 13 and 6 years of age, are cited, having nasal polyps and situs inversus. They also had suffered much from bronchitis, and the younger sister's x-ray of the chest showed opacities in the lower lobe of the left lung, as may be observed in bronchiectasis. It is emphasized that the frontal sinuses were absent in the younger sister and very small in the older sister. The variation in the symptomatology in relation to symptoms from the nose and bronchi in the family are discussed. Hereditary factors in bronchiectasis related to situs inversus are assumed to play a major role in 0.05% or in about 1% of the cases of bronchiectasis occurring in the population. The size of the frontal sinuses was investigated in cases of Kartagener's triad, situs inversus without bronchiectasis, and bronchiectasis without situs inversus. They were smallest in Kartagener's triad. This may be regarded as an indication of the influence of the genes in the particular case of bronchiectasis.

AMBERG, Rochester, Minn.

RETROLENTAL FIBROPLASIA. U. DORELLO and L. POLI, Arch. ital. pediat. e puericol. **16**:3, 1953.

During the last few years, retrolental fibroplasia, first noticed by Terry, in 1942, has reached a very high occurrence in the United States, while more and more frequent cases are reported from other countries where it had never appeared before. In view of the possibility that such a disease might occur even in Italy, more than two years of systematic investigations have been conducted by the authors.

All premature infants weighing less than 2,500 gm. received in the children's hospital of Pisa from Jan. 1, 1951, to Feb. 28, 1953, have been examined; in addition to this all children received within the years 1940 to 1950 have been checked up for control. As a result of said investigations, there was no positive evidence of any ocular modification which could be related to such a disease.

After a short summary of the most recent information about retrolental fibroplasia, eventual causes contributing to the negative results of their studies have been discussed by the authors on the basis of an accurate control of the clinical reports of the subjects.

FROM THE AUTHORS' SUMMARY.

MICROPHTHALMOS AND DEFORMITY OF THE EXTREMITIES. PAOLLO RIZZO, Riv. oto-neuro-oftal. **26**:327 (July-Aug.) 1951.

A 22-year-old single woman showed mild microphthalmos, syndactyly of the second and third toes of both feet, right internal strabismus, and decreased size of the left side of the face and the left upper limb. The fingers of the hands were small and of equal size. There were frontal hyperostosis, dextroscoliosis of the mid-dorsal region, and levoscoliosis of the lumbar region. There was a mild valgus deformity in the elbow regions. In the lower limbs, there were enlargement of the anterior part of the feet and microdactyly and isodactyly of the last four toes. The author considers this case one of a variant of Biemond's syndrome (polydactyly, mental retardation, infantilism, and hypophysial obesity). The defects are considered congenital malformations on a dysgenetic basis.

N. SAVITSKY, New York [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

KLIPPEL-FEIL'S SYNDROME. SIMON TISNADO MUNOZ, Rev. peruana pediat. **11**:129 (Oct.-Dec.) 1952.

Two cases of Klippel-Feil syndrome are reported. The patients, two male infants 2 and 3 months of age, respectively, had shortened necks, which led to the correct diagnosis by inspection alone. X-ray examination showed coalescence and flattening of cervical vertebrae, spina bifida, and absence of normal cervical lordosis. One patient maintained his head in position of torticollis because of fibrosis of the sternocleidomastoid muscle. Congenital anomalies of other skeletal segments and viscera which frequently accompany the syndrome are reviewed, and the causes of malformation are explained.

FROM THE AUTHOR'S SUMMARY.

BILATERAL CONGENITAL SYNOSTOSIS OF THE RADIUS AND ULNA: A CASE REPORT. LORENAO EXPOSITO and NILLO GOMEZ DE ROSAS, Rev. cubana pediat. **25**:171 (March) 1953.

A case is described of a 5-month-old Negro child with bilateral synosteosis of the radius and ulna. A description of the findings and functional limitations in this disorder is given.

NELSON, San Francisco.

THE PROBLEM OF PREMATURITY. RODRIGO LORIA CORTES, Rev. cubana pediat. **25**:201 (April) 1953.

Statistics in regard to many aspects of the prematurity problem for Costa Rica are presented. Comparisons are made where possible to similar statistics published in the United States.

NELSON, San Francisco.

CONTRIBUTION TO THE ETIOLOGY OF THE HEREDITARY AND NONHEREDITARY MALFORMATIONS. H. GREBE and A. WINDORFER, Deutsche med. Wchnschr. **78**:149 (Jan. 30) 1953.

Generally speaking, it is permissible to speak of human hereditary malformations only when such malformations can be demonstrated in the family. In absence of such findings the possibility of environmental factors is to be considered. The view is favored that in the majority of various embryopathies an insufficient supply of oxygen to the centers of organization may be assumed. In human teratogenesis, endogenous or exogenous injuries may produce the same effect. A few illustrative cases are described.

AMBERG, Rochester, Minn.

THE MAXIMAL TUBULAR TRANSFER OF GLUCOSE AND PARA-AMINO-HIPPURATE IN PREMATURE INFANTS. FOLKE TUDVAD and JORGEN VESTERDAL, Acta pædiat. **42**:337 (July) 1953.

The maximal tubular excretion of paraaminohippurate and the maximal tubular reabsorption of glucose has been determined in seven premature infants 19 to 135 days of age. An infusion technique was used by which it was possible to change the water administration during the experiment.

With urine flows above 3 ml. per minute per 1.73 square meter, the values of paraaminohippurate and glucose seemed to be independent of the urine flow. With lower urine flows the results were unreliable. Glucose increased with increasing age, in spite of the oldest infants being those with the lowest birth weights. The ratio, inulin clearance: glucose was higher than in adults, indicating that in the newborn premature infant the tubuli are more immature than the glomeruli. Similar changes with regard to paraaminohippurate were less evident.

FROM THE AUTHORS' SUMMARY.

ELEPHANTIASIS CONGENITA ANGIOMATOSA. HERBERT ENELL and BIRGER HAHN, Acta pædiat. **42**:416 (Sept.) 1953.

An account is given of eight cases of congenital elephantiasis with angiomatosis in which no hereditary history of the disease was found. It is emphasized that a definite diagnosis can be made by means of histological examination and that soft-tissue roentgenography may often

facilitate the diagnosis. The prognosis, with regard to spontaneous regression, is found to be poor, but the functional ability is usually relatively unimpaired. Various forms of therapy are discussed. In one of the four deaths, the cause was found to be malignancy of the growth.

FROM THE AUTHORS' SUMMARY.

Newborn

OBSERVATIONS RELATED TO NEONATAL HYPOGLYCEMIA. MURDINA M. DESMOND, J. Pediat. **43**:253 (Sept.) 1953.

Low blood sugar levels are frequently seen in newborn infants without clinical signs of hypoglycemia and despite the fact that these infants have adequate stores of glycogen. Desmond's investigation showed that premature infants respond to injections of epinephrine with a rise in blood glucose, as do full-term infants. This response is less in the first days of life than at the end of the first week. Intravenous glucose tolerance curves for both premature and full-term infants are essentially within normal limits. Serum inorganic phosphorus does not fall appreciably after the intravenous administration of glucose in the blood of newborn infants. Blood glycogen levels in the newborn period are within the normal adult range, and, within the limits of this study, no relation could be demonstrated between the eosinopenic and glycemic response of the newborn infant to injections of epinephrine.

Desmond theorizes that neonatal hypoglycemia represents a transition period between a fetal metabolism concerned primarily with storage and an extrauterine metabolism that is more concerned with energy production.

MACDONALD, Pittsburgh.

CHANGING PATTERNS OF RESPIRATION IN NEWBORN INFANTS. HERBERT C. MILLER and FRANKLIN C. BEHRLE, Pediatrics **12**:141 (Aug.) 1953.

Healthy newborn infants apparently pass through four well-defined stages of respiration. The first stage is the period during which postnatal respirations are established. This period rarely lasts more than a few minutes. It is followed by a second stage, which lasts from several hours to a day or more. During this period the respiratory rhythm in the quiet or sleeping infant is comparatively regular, regardless of the rate. The movements of the chest and abdominal walls are synchronous throughout the respiratory cycle. The excursion of the chest and abdomen is unusually uniform from one breath to another. The third stage offers a sharp contrast to the preceding one. There are many rhythms, and they are frequently irregular. The movements of the chest and abdomen are often bizarre. Sometimes the whole anterior chest wall is drawn in and downward as the abdomen expands (seesaw breathing), or the lower end of the sternum and adjacent costal margins are drawn inward as the upper chest and abdomen expand (simple retraction). There is a marked variation at times in the amplitude of the excursion of the diaphragm. There is frequent shifting of rhythms, rates, and respiratory patterns in the same infant within a matter of seconds or minutes. This stage appears to last several weeks. It is subsequently replaced by a fourth stage, in which the respiratory rhythm once more becomes regular, and the respiratory patterns lose their bizarre character. The movements of the chest and abdomen become synchronous, although there may be retraction at the lower end of the sternum during inspiration.

Knowledge of the characteristic pattern in Stage 2 is of help in making a clinical evaluation of the baby's condition. If the infant in this stage is quiet or asleep and is breathing with a regular rhythm and with synchronous movements of the anterior chest and abdominal walls, no difficulties are to be expected. The presence of retraction of the lower end of the sternum and adjacent costal margins in this stage, even if it is minimal in amount, has been, in the authors' experience, often associated with serious illness and a high mortality rate. Further study will be needed before a final evaluation can be given of the full significance of retraction of this kind.

One of the differences between Stages 2 and 3 is an increasingly vigorous contraction of the diaphragm in Stage 3. This factor is thought in part to account for the appearance of "seesaw" breathing and "simple retraction" in Stage 3. "Seesaw" respirations are seen only in about 4 to 5% of infants less than 24 hours old; it can be said that the infant either is potentially ill or has entered upon Stage 3 sooner than most infants. On the other hand, "simple retraction"

is not to be considered a normal finding in the first 24 hours of life. Its presence in that period is evidence of some cardiorespiratory difficulty. After 24 hours of age "simple retraction" begins to make its gradual appearance as a normal finding and as a result of increased diaphragmatic activity.

Further investigation is needed before a complete explanation can be given of the various stages of respiration described above.

FROM THE AUTHORS' SUMMARY.

FLUID AND ELECTROLYTE PROBLEMS IN THE NEWBORN. KATE CAMPBELL, M. J. Australia **2**:201 (Aug. 8) 1953.

Differences between electrolyte patterns of adults and infants are outlined. Physiological differences in electrolyte balance control are indicated, with a discussion of their effect on the proper treatment of fluid and electrolyte imbalance.

McGUIGAN, Evanston, Ill.

CONGENITAL OR NEO-NATAL THROMBOCYTOPENIC PURPURA. S. E. STENING, M. J. Australia **2**:210 (Aug. 8) 1953.

The author classifies neonatal thrombocytopenic purpura into three groups: (1) infants born of mothers with thrombocytopenia, (2) affected infants born of normal mothers without evident etiologic factors, (3) affected children with purpura due to toxic, poisonous, or infective process acquired either intrauterine or extrauterine. Group 1 is the only true congenital type. Since the disease is due to factors transmitted across the placenta, it is self-limited once these factors are eliminated after birth.

Treatment varies with the type. In Group 1, replacement transfusion is effective. Group 2 requires transfusions, corticotropin (ACTH) or cortisone, and splenectomy if the course is severe. Group 3 requires elimination of the causative factors plus transfusion.

McGUIGAN, Evanston, Ill.

CARBONIC ANHYDRASE IN NEWBORN AND INFANTS. RAGNAR BERFENSTAM, Études néo-natales **2**:21 (March) 1953.

After a review of the properties of carbonic anhydrase, the author discusses the problem of whether the low enzymatic activity of this enzyme in the blood of premature infants has any adverse effect upon their vital functions.

The enzymatic activity was measured by the manometric method described by Meldrum and Roughton (measurement of the rate of formation of CO_2 from a solution of bicarbonate at a given pH in the presence or absence of the enzyme), and in the newborn it was found to be about one-third of that in the adult. In premature infants it was considerably less, ranging from 3 to 5% of the adult rate in the smallest to 10 to 15% in bigger babies. Blood transfusion or intramuscular injections of blood increase the enzymatic activity (maximum in 4 hours, persisting for 24 hours). The increase is due to a thermostable, dialyzable, and nonelectrolytic factor in the plasma.

There is a relationship between the activity of the enzyme and the amount of zinc in the blood, but raising the zinc content of the red blood cells is not accompanied by increase in enzymatic activity.

The significance of the low enzymatic activity in the blood of premature infants is discussed. No definite answer can be given in the present state of knowledge.

FROM THE AUTHOR'S SUMMARY.

BILIARY CIRRHOSIS AND HEMOLYTIC DISEASE OF THE NEWBORN. G. PARRINELLO, Clin. pediat. **35**:341 (May) 1953.

The case of an 11-month-old girl with biliary cirrhosis of the liver, splenomegaly, and hemolytic anemia with erythroblastosis is reported with autopsy findings. This was the third child of this family to die of this condition in infancy. This case suggests the possibility that infants with erythroblastosis fetalis may also be subject to biliary cirrhosis.

HIGGINS, Boston.

"Rooming-In" in Uruguay. Antonio Stabile and Carlos A. Bauza, Arch. pediat. Uruguay **24**:173 (March) 1953.

A survey on newborn practices was made in 23 rural community hospitals and 12 obstetric services in the metropolitan area. Rooming-in was performed in 32 hospitals; the newborns stayed in the nursery in 3 hospitals. The objectives and advantages of rooming-in are reviewed, and, in view of the increasing rhythm of hospital building, a very careful consideration of the subject is advised before making any change in this traditional hospital arrangement for mothers and their newborn infants. Mental health aspects are stressed.

From the Authors' Summary.

Late Prognosis in Asphyxia Neonatorum. B. Hellstrom and B. Jonsson, Acta pædiat. **42**:398 (Sept.) 1953.

Eighty-five children treated at a children's hospital for asphyxia neonatorum were subjected to a follow-up examination. Eighteen died during the newborn period. Sixty-five of the 67 survivors were followed up. Among them, 18 showed signs of a permanent cerebral injury (spasticity, mental retardation, convulsions). The late prognosis was correlated to different clinical symptoms during the newborn period. Children with convulsions, changed tonus, bulging fontanel, or reduced sucking capacity have a conspicuously bad prognosis.

From the Authors' Summary.

Acute Contagious Diseases

Relation Between Personality Factors and Fatigue in Severe Poliomyelitis. Jacob H. Conn, A. M. A. Arch. Neurol. & Psychiat. **70**:310 (Sept.) 1953.

Fourteen patients from 14 to 35 years of age are presented All had an unadaptive rigid personality development. They were all outwardly happy, well adjusted, physically healthy, and more active than average but lacked aggressive self-assertion, and were overly conscientious and anxious to be accepted. As a result, they continued activity to the point of fatigue before giving in to the signs of poliomyelitis, and all were severely paralyzed.

McGuigan, Evanston, Ill.

The Cardiovascular System in Acute Infectious Disease. Irving Fine, California Med. **79**:311 (Oct.) 1953.

Myocarditis may result from a wide variety of acute infectious diseases, but electrocardiographic abnormalities interpreted as indicating myocarditis may arise from a number of other causes.

Among the factors which may cause myocarditis are direct invasion by an organism, the toxic products of an organism, hypersensitivity to the products of an organism, drugs used in therapy, deficiency in nutrients, electrolyte imbalance, and, rarely, fever.

Recently emphasis has been placed on the finding that circulatory failure in acute infectious diseases is often primarily peripheral, although heart failure due to myocarditis is not uncommon.

Pryor, Redwood City, Calif.

Rehabilitation—Prescription for Living. Hart E. Van Riper, Illinois M. J. **102**:300 (Nov.) 1952.

In this presentation some of the physician's responsibilities to disabled patients after they are discharged from definitive medical care are enumerated.

It is estimated that there are in this country today more than 2,000,000 persons who, with proper care and with the intelligent bringing-to-bear of all disciplines that are known and available, could be made useful and productive members of society. Added to this large number of disabled or handicapped persons, it is estimated that there are approximately a quarter of a million new handicapped persons in one year.

The incidence of poliomyelitis has markedly increased the last few years. About 20% of the cases are left with some permanent physical handicap. Last year over 15% of the cases that were hospitalized remained in the hospital for more than 90 days. Many of them in that 90-day period received little, if any, attention toward their future possibilities to regain their capacity for more nearly normal living. Except in those few communities that have established rehabilitation centers, most of these persons are prisoners of their handicaps.

When physicians think of the disabled person in the sheltered workshop or homebound, they are exaggerating that person's disability, rather than emphasizing those assets that remain to him, which leave him as capable of carrying on a normal existence as before his accident or illness.

According to Van Riper, private patients and those that are being paid for by chapters of the National Foundation are today paying for rehabilitation in many hospitals, and what they are paying for is nothing more than a little bit of physical therapy. There are only a few institutions today that have a complete program of rehabilitation. For such a program there should be a responsible director who is, above all else, a good physician, a person who is aware of all of the social complications that come with disease and injury. In a true rehabilitation center the work that is done should be spent in trying to make the person able to carry on for himself. It is necessary to evaluate patients in terms of what elements of daily living they can do for themselves and then set out doing what can be done to correct those deficiencies to the point where they can act and do for themselves. Many of the disabled persons who have lost some of their faculties seem to have developed the others even to a greater point of acuity than one would normally expect. Job counseling and placement are exceedingly important.

The cost of a good rehabilitation program is not cheap. Yet, economically, the results of utilizing such a rehabilitation program for city welfare cases in New York has resulted in a decrease in total hospitalization of patients. In the end, more patients are discharged from the hospitals, off the welfare rolls, and gainfully employed in their own or some other profession or business which has been deemed best suited for them. With increasing taxes and costs of living, a recent survey in one of the eastern communities has shown that more and more of the aged and disabled are being transferred to the welfare rolls. So that in the end, government as well as voluntary agencies would do well to think more and more of returning the physically handicapped to a gainful place in life.

BARBOUR, Peoria, Ill.

AIRWAY MANAGEMENT IN PATIENTS WITH POLIOMYELITIS. HAMILTON S. DAVIS and HAROLD F. BISHOP, J. A. M. A. **149**:1175 (July 26) 1952.

There is a trend toward early use of prophylactic tracheotomies in the treatment of acute anterior poliomyelitis with severe respiratory involvement. Davis and Bishop propose the formation of a team composed of appropriate representatives of the medical or pediatric, neurologic, otolaryngologic, and anesthesiologic services. Such a team could adequately evaluate each case, paying special attention to respiratory complications.

In 1948, out of six bulbar cases there were two deaths, both having been treated with late tracheotomies. In 1949, out of seven children with bulbar poliomyeliits there were four deaths, all four having been treated with early tracheotomies. In this epidemic, out of 11 adults 5 died, most having been treated with early tracheotomies, and most showing evidence of pulmonary complications and central nervous system failure on autopsy.

The 1949 epidemic was much more virulent. It is very difficult to evaluate results because of the variability of the epidemics.

KIMBALL, Evanston, Ill.

RUSSIAN SPRING-SUMMER ENCEPHALITIS. G. A. JERVIS and G. H. HIGGINS, J. Neuropath. & Exper. Neurol. **12**:1 (Jan.) 1943.

Russian spring-summer encephalitis is a disease endemic in certain far-eastern provinces of Russia. In man three clinical forms are recognized: (*a*) abortive infections, causing fever for three to five days and ending in full recovery; (*b*) meningoencephalitic forms of moderate severity, followed by recovery in 80% of cases and by permanent neurological sequelae in 20% and (*c*) severe fulminating meningoencephalitis, with death usually occurring within one to seven days.

The disease is caused by a virus. The vector of the virus is a tick, and possible natural reservoirs of infection are small rodents and birds. No reports of the disease in the human have appeared outside of Russia.

The authors describe a patient who contracted Russian spring-summer encephalitis while engaged as a laboratory assistant in experimental work intended to investigate the effect of Russian encephalitis virus upon experimental tumors in mice. The patient fed and handled the infected animals under strict precautions usually carried out in this type of work. At no time did she report any laboratory accident, such as puncture wound or breaking of a virus ampule.

The clinical picture presented was one of rapidly fatal acute encephalitis and corresponded closely to the fulminating form of spring-summer encephalitis described by the Russian investigators. The sudden death, which occurred on the fourth day of illness, suggested bulbar involvement. The results of neutralization tests showed that the virus isolated from brain material of the patient was identical with Russian spring-summer encephalitis virus.

The pathological examination indicated a widespread involvement of the gray matter, with selectivity of the lesions for the motor cortex, cerebellum, medulla, and spinal cord. The authors point out the similarities between the lesions of Russian encephalitis and those experimentally produced by louping-ill virus.

ALPERS, Philadelphia [A. M. A. ARCH. NEUROL. & PSYCHIAT.].

ACUTE POLIOMYELITIS. EMIL SMITH, IRWIN L. HARRIS, and PHILIP ROSENBLATT, J. Pediat. **43**:9 (July) 1953.

The authors report their experiences in the 1950 poliomyelitis epidemic. They review 263 cases. More than 25% of their cases were nonparalytic, 22.7% were bulbar, and 50.4% were spinal. The over-all mortality rate was 8%. The virulence of the disease varied from month to month.

In general, death in poliomyelitis was the result of bulbar involvement. The authors propose that pulmonary angiospasm may be the underlying cause of death in these cases. Tracheotomy is of value only when there is tracheobronchial obstruction. This is usually not present in bulbar poliomyelitis. Vasodilator drugs, notably benzazoline (Priscoline), may temporarily relieve symptoms in some cases.

MACDONALD, Pittsburgh.

THE TREATMENT OF DIPHTHERIA AND DIPHTHERIA CARRIERS WITH TERRAMYCIN. SEETA LALL and SAMUEL KARELITZ, J. Pediat. **43**:35 (July) 1953.

Lall and Karelitz gave oxytetracycline (Terramycin), 50 mg. per kilogram of body weight per day, along with diphtheria antitoxin, to six cases of acute faucial diphtheria. Oxytetracycline shortened the period of positive throat cultures, as compared with cases receiving antitoxin alone.

Six carriers were given oxytetracycline, with prompt removal of Corynebacterium diphtheriae from their throat cultures. The authors conclude that oxytetracyline is at least as effective as penicillin or chlortetracycline (Aureomycin) in removing diphtheria organisms from the respiratory membranes of acute cases of diphtheria and diphtheria carriers.

MACDONALD, Pittsburgh.

INCIDENCE OF HYPERTENSION IN POLIOMYELITIS. MEYER A. PERLSTEIN, MORTON B. ANDELMAN, DAVID C. ROSNER, and PAUL WEHRLE, Pediatrics **11**:628 (June) 1953.

Hypertension is a frequent occurrence in poliomyelitis. In a 1950 epidemic in Chicago it occurred in about one-third of all cases.

Hypertension was generally of transitory nature, although in two instances it was prolonged.

Hypertension was three times more frequent in cases with paralysis than in nonparalytic cases. It was commonest in respirator cases.

The incidence of hypertension was not related to the localization of paralysis, emotional factors, anoxia, sympathetic system involvement, or kidney involvement. Therefore, it is inferred that it is probably of central origin.

FROM THE AUTHORS' SUMMARY.

POLIOMYELITIS VIRUS IN HUMAN BLOOD DURING THE "MINOR ILLNESS" AND THE ASSYMPTOMATIC INFECTION. DOROTHY M. HORSTMANN and ROBERT W. MCCOLLUM, Proc. Soc. Exper. Biol. & Med. **82**:434 (March) 1953.

Three children, 10, 4, and 3 years of age, in the same family developed febrile illnesses, while the fourth child, 2 years of age, remained well. The father, 37 years of age, had a headache the day before but no other symptoms, and the mother remained well. The symptomatology was compatible with the diagnosis of abortive poliomyelitis. Throat swabs, rectal swabs, and blood specimens were collected from the four children. Poliomyelitis virus was isolated from the blood in all four children. Virus was present also in the throat and rectal swabs. All strains proved to be Type 1 (Brunhilde). None of the children went on to develop signs or symptoms of major illness, either paralytic or nonparalytic.

HANSEN, Galveston, Texas.

POLIOMYELITIS IN INFANTS UNDER THE AGE OF SIX MONTHS. A. A. MCCONNELL, Arch. Dis. Childhood **27**:121 (April) 1952.

Ten cases of poliomyelitis in infants under the age of 6 months are described in detail. These occurred during the 1950 epidemic in Northern Ireland.

The ages of the patients varied from 16 days to 5 months. Symptoms were fever, vomiting, anorexia, and irritability. Paralysis was present in all cases. One patient recovered completely. Wasting and contractures developed in several patients, and three patients died.

KELLY, Milwaukee.

THROMBOCYTOPENIC PURPURA FOLLOWING MEASLES. O. D. FISHER and T. M. KRASZEWSKI, Arch. Dis. Childhood **27**:144 (April) 1952.

Two cases of thrombocytopenic purpura following mild attacks of measles are described. Agranulocytosis developed in one patient during the acute hemorrhagic phase. Bone-marrow examination in both instances demonstrated the presence of normal megakaryocytes. Attention is drawn to the association of thrombocytopenic purpura and the acute infectious fevers.

POLIOMYELITIS WITH MYOCARDITIS, COMPLICATING STILL'S DISEASE. R. C. B. PUGH, Great Ormond St. J. **4**:118 (Dec.) 1952.

Poliomyelitis occurred, unsuspected before death, in an advanced case of Still's disease. Postmortem examination showed extensive pericarditis and myocarditis, with typical findings of poliomyelitis in the central nervous system. The authors present evidence to show that the myocarditis was due to the virus.

MCGUIGAN, Evanston, Ill.

COXSACKIE VIRUS INFECTIONS IN AUSTRALIA, WITH SPECIAL REFERENCE TO THEIR EPIDEMIOLOGY. N. F. STANLEY, M. J. Australia **2**:216 (Aug. 8) 1953.

Coxsackie virus infections are common throughout the Western Pacific area, as shown by antibody response in human sera. No correlation between poliomyelitis and coxsackie infections could be demonstrated by the study.

MCGUIGAN, Evanston, Ill.

INSPIRATORY SWELLING OF THE SUPRAHYOID REGIONS IN POLIOMYELITIS. P. SÉDALLIAN, F. JOURDAN, A. BERTOYE, C. EXBRAYA, G. MADONAT, and P. PAZAT, Presse méd. **60**:1 (Jan. 5) 1952.

The authors draw attention to a sign of diagnostic value in early bulbar poliomyelitis occurring before the classic signs of bronchial hypersecretion, respiratory weakness, and difficulty in swallowing. With each inspiration, a swelling appears beneath the jaw, similar to the inspiratory movement of that area in frogs. Since its appearance precedes the onset of asphyxia by some time, procedures may be undertaken to treat symptoms in an early stage.

Experiments were conducted to determine the pathological changes causing this phenomenon. The authors conclude that the lesion must lie in the region of the nucleus of the solitary fascicle.

DAFFINEE, Melrose, Mass.

POLIOMYELITIS AND DRINKING WATER. P. LEPINE, J. BOYER, and H. SAPIN-JALOUSTRE, Presse méd. **60**:1057 (July 19) 1952.

Propagation of poliomyelitis by contaminated drinking water has been considered to be possible. Since almost all towns in France get their water supply from rivers, especially such a large city as Paris, it would have been likely to observe here a higher incidence of poliomyelitis than elsewhere, in spite of the sterilization widely and strictly applied to the drinking water by the municipality of the towns.

The study carried out by the authors has shown the morbidity of poliomyelitis to be about the same in sectors supplied with water from the Seine River and from the Marne River or from springs.

Any focus of the disease has never been exactly in relation to the distribution of the water.

It is, however, not impossible that the water after being sterilized might contain some poliomyelitis virus but in so small an amount that this contributes to an occult immunization of the population.

It seems that none of the cases of poliomyelitis which has been contracted in the Parisian region has been transmitted by the water of the city. Perhaps the spread of the disease is produced through tainted food, especially green vegetables. In conclusion the purification of the water as carried out by the city of Paris is sufficient as regards the prophylaxis of poliomyelitis.

FROM THE AUTHORS' SUMMARY.

CLINICAL ASPECT OF AN EPIDEMIC OF POLIOMYELITIS IN FRENCH OCEANIA: SIGNIFICANCE OF INTRAMUSCULAR INJECTIONS IN THE ETIOLOGY OF PARALYSIS. G. THOORIS and L. ROSEN, Presse méd. **60**:1712 (Dec. 17) 1952.

An epidemic of poliomyelitis broke out in French Oceania in January, 1951, with its peak in April and end in July, with 109 cases in Tahiti and 29 in the other islands and nine fatalities.

The largest number of cases was seen in the eastern part of Tahiti. A few cases had previously appeared in 1947 and 1950. The clinical picture was typical with, however, a prevalence in paralysis of the lower limbs (nine in lower limbs against two in upper limbs). Within six months of onset of symptoms 19% of the patients were still showing paralysis and 23% a reduction in motion potency. Children were most affected; the majority of them had received intramuscular injections of arsenic, bismuth, or mercury (each substance either alone or associated with the others) during the month prior to the onset of the paralysis. It appears that these injections had favored the occurrence of the paralysis, its selective location in the lower limbs, and its severity. The type of chemotherapeutic agent did not seem to have any bearing on the number of paralysis cases, their distribution according to age, their location, or their severity. Attention is also called to the fact that, before the occurrence of poliomyelitis in Tahiti, an epidemic of measles had broken out (January and February, 1951), so that all children affected by poliomyelitis had previously had measles; the fact is of interest because of the well-known epidemiologic similarity of the two diseases.

FROM THE AUTHORS' SUMMARY.

RUBEOLA AND PREGNANCY. P. HAUDUROY, Bull. schweiz. Akad. med. Wissensch. **8**:537 (Nov.) 952.

The severe embryopathology which results from a rubeola infection of the mother during pregnancy are well known. An attempt was made to discover how frequent such cases are by means of a questionnaire sent out to all Swiss doctors.

In 1949, 77 definitely diagnosed cases were reported from observations made during the preceding four to five years. Of these 22 (possibly 24) there was definitely embryopathology of a severe degree. Three women had aborted, and in nine more the pregnancy was interrupted. There were 38 abnormal children born. When the mother falls ill with rubeola in the first and second months of pregnancy, there is at the most a 12 to 16% probability of the child being normal. From the fifth month on, there is no more danger for the child. Owing to the severity of the malformations, it is thought that an alteration of paragraph 120 of the Con-

federal Criminal Law should be made to recognize the indication from the point of view of the child for an interruption of the pregnancy. Owing to the relative infrequency of embryopathology, the author does not press this recommendation.

FROM THE AUTHOR'S SUMMARY.

LIMITS AND RELATION OF NERVOUS LOCALIZATIONS AND OUTER NEUROSES IN DISEASE CAUSED BY THE POLIOMYELITIS VIRUS. A. LEONE, Ann. ital. pediat. **5**:347 (Oct.) 1952.

The author, after a short review of the problem of nervous and extranervous localizations of Heine-Medin disease, writes about the non-nervous forms of such disease in Cagliari Clinic during 20 years. In about a fourth of the patients (22.48%), in different epidemic episodes, some onsets which could not be considered secondary to the nervous lesions from the virus, were observed during the acute period of the poliomyelitic process. Above all, onsets in digestive apparatus (11.51%) and respiratory apparatus (7.29%) were the most important, while cutaneous onsets (0.56%), and cardiocirculatory onsets (0.98%), etc., were practically negligible. The author points out that the enteric as well as the respiratory phenomena disappeared after therapy with convalescent serum, while the patients did not experience any effects from the administration of sulfonamides and antibiotics. This strengthens the idea of etiology from virus of Heine-Medin disease of the extranervous forms.

FROM THE AUTHOR'S SUMMARY.

CHANGES IN THE BLOOD AND BONE MARROW CYTOLOGY AND IN THE BLOOD PROTEIN CONTENT IN CHILDREN WITH WHOOPING COUGH UNDER TREATMENT WITH CHLORAMPHENICOL. T. PORCELLI, Clin. Pediat. **34**:241 (April) 1952.

Excellent therapeutic results were obtained in the treatment of 19 children with whooping cough by the use of chloramphenicol; no toxic effects from the use of this drug were observed.

Chemical and cytological observations of the blood were made before and 10 to 50 days after the drug had been given. The following significant changes were found: The erythrocyte sedimentation time was diminished, the number of erythroblasts in the bone marrow and of monocytes in both the bone marrow and the blood smears was increased and there was an increase in the serum globulin, sufficient in some cases to cause an inversion of the albumin-globulin ratio.

HIGGINS, Boston.

THROMBOPENIC PURPURA OCCURRING WITH JENNERIAN VACCINATION. G. PANZETTI, Lattante **23**:37 (Jan.) 1952.

A baby 9 months of age developed purpuric spots, a high fever, toxicity, and enlarged glands, beginning on the fourth day after vaccination for smallpox. There was the usual successful vaccination take. The child's blood showed a relative lymphocytosis, 100,000 platelets, and a bleeding time of four and one-half minutes. On the 10th day, the child's condition began to improve, and by the 20th day the child had recovered. Purpura is a very rare complication of vaccination. Its appearance may be analogous to purpuric smallpox. As the infant was rachitic and below par nutritionally at the time of vaccination, the author recommends that vaccination be postponed, if possible, until a baby is in good physical condition.

HIGGINS, Boston.

TREATMENT OF WHOOPING COUGH BY THE INHALATION OF STREPTOMYCIN. E. EGIDI, Minerva pediat. **4**:250 (April 15) 1952.

At the pediatric clinic in Turin, 163 patients with pertussis have been treated with an apparatus in which a solution of streptomycin is sprayed into a box and then inhaled by the patient. Blood analyses for streptomycin showed satisfactory absorption. This procedure led to excellent therapeutic results in 80% of the cases and is also recommended as safe and readily accepted by the patients.

HIGGINS, Boston.

VIRUS NEUTRALIZATION TEST FOR POLIOMYELITIS IN THE POPULATION OF SANTIAGO (CHILE). BENJAMIN VIEL and FEDERICO CATTANEO, Rev. chilena pediat. **22**:327 (Aug.) 1951.

The existence of specific Lansing antibody was demonstrated in the normal population of Santiago.

The presence of the specific antibody in the population of Santiago increases proportionally with age, reaching its maximum between 5 and 15 years; the percentages found are in agreement with those given by the majority of authors.

The neutralization test in Lansing strain adapted to the white mouse has no diagnostic value in doubtful cases.

In the recent poliomyelitis epidemic in Santiago, the Lansing virus strain adapted to the white mouse does not seem to have been greatly involved.

FROM THE AUTHORS' SUMMARY.

CONTRIBUTIONS TO THE EPIDEMIOLOGY OF DIPHTHERIA. HERNAN ROMERO, J. M. BORGONO, M. CERVANTES, E. DUSSERT, R. HUERTA, N. KLIWADENKO, and J. VILDOSOLA, Rev. chilena pediat. **23**:277 (July) 1952.

For the moment the morbidity and mortality for diphtheria are low compared with other diseases. Nevertheless, the problem is one that should give food for thought, as the changes over the last 45 years suggest an increase.

A serious problem is the relatively insufficient protection that is given with toxoid vaccination, which, added to the apparent lack of carriers and the high percentage of Schick positives, suggests that the population is losing its basic immunity. Immunization could contribute to reestablishment of the disease. The finding of strains different from the usual ones and which have proved to be toxic can also be taken as an alarming manifestation. To prove this fact, it might be useful to employ on a larger scale the in vitro tests that the Bacteriological Institute is successfully trying out.

The Quilpue epidemic which was not stopped by the first vaccination program started a second one, the characteristics of which are described. The morbidity and mortality reached have been extraordinarily high.

Controls on purchasing antitoxin and antibiotics have improved the reporting of diphtheria which is still very effective, and that only as an exception originates from the doctor treating each case. In Santiago, the treatments on the whole are timely and sufficient.

The high proportion of secondary cases, especially in well-to-do families, can be the consequence of a lack of reporting and lack of isolation, quarantine, and immunization of contacts, which is the consequence of non-reporting.

FROM THE AUTHORS' SUMMARY.

CLINICAL STUDY OF FIFTEEN CASES OF ENCEPHALOPATHIC PERTUSSIS. MARIANO LATORRE and OSCAR PEREZ, Rev. chilena pediat. **23**:300 (July) 1952.

The classic concepts of encephalopathic pertussis are reviewed. Fifteen cases are then analyzed from the initiation, symptomatology, progress, and prognosis points of view. The sequelae are also mentioned. There is a summary on the pathology of the cases in which the patients died.

FROM THE AUTHORS' SUMMARY.

SMALLPOX VACCINATION. DIEGO F. SOSA BENS, Rev. cubana pediat. **25**:100 (Feb.) 1953.

The author reviews the history of vaccination, kinds of vaccine, and indications for vaccination, as well as techniques and complications of smallpox vaccination.

NELSON, San Francisco.

TYPHOID AND PARATYPHOID VACCINE. ARTURO CURBELO, Rev. cubana pediat. **25**:120 (Feb.) 1953.

The incidence of typhoid fever, broken down according to age and month of occurrence, is given for the contagious disease hospital "Las Animas" for the years 1940, 1949, 1950, and 1951. The total number of cases has been decreasing, but the percentage of cases occurring under the age of 14 years has been increasing.

The preparation and methods of administration of typhoid and paratyphoid vaccine are discussed. The author believes that in Cuba typhoid vaccination should be started at about the second year of life.

NELSON, San Francisco.

VACCINATION AGAINST RABIES. JUAN MARIA GONZALEZ HERNANDEZ, Rev. cubana pediat. **25**:157 (March) 1953.

The author describes the methods used for antirabies vaccination in Cuba. Of interest is his impression of the value of thiamine hydrochloride in large doses in the prevention of untoward reactions with such vaccination.

NELSON, San Francisco.

PASSIVE IMMUNIZATION BY PLASMA DERIVATIVES: CLINICAL APPLICATION OF GAMMA GLOBULIN. ALVARO SILVA, Rev. cubana pediat. **25**:163 (March) 1953.

A summary of the history of the fractionation of blood is made. The various fractions of human serum that have been obtained are mentioned, and the author goes on to describe the prophylactic use of gamma globulin in various diseases.

NELSON, San Francisco.

HEPATOSPLENIC MANIFESTATIONS DURING A SPECIAL COURSE OF ACUTE ANTERIOR POLIOMYELITIS. H. KALK and I. FAUST, Deutsche med. Wchnschr. **78**:1014 (July 17) 1953.

Among 21 patients admitted with acute poliomyelitis were 5 who presented enlargement of liver and spleen at various periods from the onset of the disease. In four cases, including a 13-year-old child, this happened from the 30th to the 56th day, and in one, a 3-year-old child, on the 7th day. On biopsy of a specimen of the liver, lesions of the reticuloendothelial system were found with occasional periportal infiltration with round cells and histiocytes. Only two of the cases had a slight icterus, and no marked deviations of functional tests were encountered in any. Liver and spleen receded in a few days to a few weeks.

AMBERG, Rochester, Minn.

THE QUESTION OF LIVER DAMAGE DURING SCARLET FEVER. HEINRICH WIESENER, Monatsschr. Kinderh. **100**:389 (Sept.) 1952.

During the first few days of scarlet fever urinary urobilinogen in the form of increased stercobilinogen and indican values was noted. No increased serum bilirubin levels were found. Electrophoretic serum protein studies, nonprotein nitrogen, blood lipids, cadmium sulfate tests, galactose, and bilirubin tolerance tests were all normal. On the basis of these studies it was not felt that liver damage occurs during scarlet fever.

HARTENSTEIN, Milwaukee, Wis.

STUDIES ON DIPHTHERIA. BO VAHLQUIST and FOLKE NORDBRING, Acta pædiat. **41**:53 (Jan.) 1952.

Fifteen premature infants were inoculated with single doses of diphtheria toxoid between the 1st and the 10th day of life. After 4 to 5 weeks only 6 of 14 children showed a weak reaction, after 12 weeks 12 of 14 children had responded, but the median titer was only 0.008 antitoxin units per milliliter. The effect was weaker than that previously obtained by vaccination of full-term children.

FROM THE AUTHORS' SUMMARY.

REINFECTIONS WITH MEASLES, FAMILIAL IMMUNITY DEFECT. ERIK THAMDRUP, Acta pædiat. **41**:276 (May) 1952.

Authentic reports on reinfection with measles are rare. The author reports a case of presumably fourth infection with measles in an 8-year-old boy who had also had whooping cough and German measles twice, and, further, recurring tonsillitis and "influenzal infections." The patient's mother, two of her sisters and brothers, and a brother had had measles twice; the brother also had had whooping cough twice.

Examinations of the patient's serum proteins showed a normal content of total protein, albumin, and globulin. The electrophoretic pattern was normal. Diphtheria and tetanus anti-

toxins could not be demonstrated in the patient's blood. Parotitis complement fixation was 4. Antibody against influenza A could be demonstrated. After vaccination against diphtheria and tetanus, a normal formation and excretion of antitoxins was ascertained (followed for a year). The electrophoretic pattern remained unchanged. Previous communications and the anamnestic information received about this patient seem, however, to indicate that there are persons who have a poor immunization capacity against measles (in this patient also against certain other infections) and that this is a constitutional hereditary property.

FROM THE AUTHOR'S SUMMARY.

DISCUSSION OF THE VARIOUS FACTORS, PARTICULARLY PENICILLIN TREATMENT, AFFECTING THE INCIDENCE OF MYOCARDITIS. LEVANDER-LINDGREN, Acta pædiat. Suppl. 91, 1952.

The purpose of this work has been to study the effect of penicillin on myocarditis associated with scarlet fever. This has been done by means of electrocardiographic examinations on concurrent groups of patients with scarlet fever treated both with and without penicillin. To accomplish this it has been necessary to make a thorough study of the electrocardiograms in order to differentiate between alterations resulting from acute myocarditis and others caused by physiologically normal variations, constitutional anomalies, or old lesions.

The material consists of 450 cases of scarlatina treated with penicillin, 440 controls who received no penicillin, and a concurrent group of 211 in whom the initiation of penicillin was delayed until the fifth hospital day. In addition there are two later treatment groups consisting of 707 patients, together with an incomplete control group of 99. These cases, as well as a number in the desquamating stage and others with scarlatina from the same period, have also been included, since they are of interest with regard to the electrocardiographic studies. Altogether the material includes 2,831 patients, of whom 279 were adults.

The following general principles have been observed in evaluating the material: 1. Electrocardiograms have been recorded serially and each series evaluated individually. 2. Even in patients whose hearts are not affected, the electrocardiograms can be expected to vary more than ordinarily during an infectious illness with its different phases of sympathetic and vagus influence. 3. The normal electrocardiogram of the person can be established after recovery (as a rule the myocarditis of scarlet fever is reversible). Stimulation of the sympathetic and vagus factors, "work"-electrocardiograms, and recordings of the electrocardiogram in various body positions have been employed in this connection to study the normal variability in different subjects. 4. A pathological alteration in the electrocardiogram can be considered to justify a diagnosis of myocarditis only if an association with the scarlatina can be demonstrated. On the other hand, a variation within the accepted normal limits may be an indication of myocarditis if it lies beyond the normal limits of variability for the subject in question. 5. Alterations apparently within physiological limits may also be due to a myocarditis. If, in addition, subjective cardiac complaints have been reported, the patient has been included in a special group designated by "probable myocarditis with equivocal electrocardiographic changes and heart symptoms."

Electrocardiographic findings were as follows: Alterations of the P-wave have been analyzed. The majority of these alterations were apparently due to minor changes in the position of the pacemaker (called "perisinus rhythms" by the author) and are physiologically normal in character. A definite intra-auricular conduction disturbance was present in only one case. Coronary sinus rhythm or arterioventricular nodal rhythm have been observed in 43 cases. These have been analyzed with reference to whether they showed signs of being active or passive and whether they were associated with the scarlet fever. Of these cases, eight were definitely active and have been interpreted as evidence of myocarditis, while three were of questionable nature. The others give the impression of having been passive physiological wandering of the pacemaker associated with decreasing sinus frequency or increased vagus effect. Premature systoles have been observed in 31 patients. Although five of these were pathological in character, only one of them displayed a definite association with a scarlatina myocarditis. Parasystoles of the ventricular type have been diagnosed in five patients and in one of them the cause seems to have been a myocarditis. Escaped beats of nodal origin have been observed in nine patients. Ventricular escaped beats were seen in two cases, both of whom have been considered to have myocarditis. Auriculoventricular conduction disturbances have been regarded as resulting from

myocarditis in 34 patients. Among these were one case of total block and two of Grade-II block. Four of the subjects with myocarditis had P-Q values within accepted normal limits, but the range of variation and the over-all series of electrocardiograms in these cases indicated a temporary disturbance during the illness. Another 26 patients were found to have prolonged P-Q intervals, and 12, large variations in the P-Q time, although these remained unaltered over a period of one or several years. In three different families two or three siblings displayed prolonged P-Q times, and a constitutional anomaly is regarded as the probable explanation.

Changes in the T wave of various degrees which have been interpreted as evidence of a scarlatina myocarditis have been observed in 57 cases, and depression of the S-T segment with the same significance have been found in 11 patients. In another large group of patients the alterations were found to have a possible connection with sympatheticotonic factors or changes in position. Intraventricular conduction disturbances have been observed in 29 patients, but in only two cases, both of whom displayed an intermittent Wilson block, would a scarlatina myocarditis seem to have been the explanation. The remaining cases displayed no change during a long period of observation. Two pairs of siblings displayed similar alterations seeming to indicate the presence of a constitutional anomaly. Preexcitation was found in seven cases, although in only one did it appear to be related to the scarlet fever.

The results with regard to the incidence of myocarditis were as follows: Certain cases of myocarditis with more marked changes in the electrocardiograms have been designated as "severe." The effect of the frequency with which the electrocardiograms are recorded is demonstrated by the fact that the incidence of myocarditis diagnosed in a group of 208 patients rose from 3.9% when the electrocardiogram was recorded once a week to 5.8% when three recordings were made each week. The age factor is illustrated by the significantly higher total incidence of myocarditis in adults than in children (11.5% as compared with 3.1%), as well as the more "severe" electrocardiographic changes (5.0% compared to 0.24%). Seasonal variations during a year were apparent. The author found that children have a higher incidence of myocarditis during the winter season than during the summer. The same tendency was displayed by the adults. A comparison between the cases receiving penicillin and the controls revealed that all groups of adults and all but one group of children receiving penicillin early in the illness had a lower incidence of myocarditis than the control groups. In the adults a statistical analysis of the individual groups revealed no significant difference. When two penicillin groups and their controls were combined the difference in the incidence of myocarditis between the penicillin cases and the controls rose to $11.8 \pm 5.5\%$. With regard to "severe" alterations the difference was a probable $9.4 \pm 3.8\%$. Patients who began to receive penicillin later in the illness reveal a higher incidence of myocarditis than those receiving early treatment but a lower one than the controls. The incidence of "severe" electrocardiographic changes in all of the adults receiving early penicillin treatment in the entire study is 0.84%, while in all other adults, controls, desquamators, and those receiving late penicillin treatment, the incidence was 8.8%. This difference is statistically significant. In children the differences do not come to a statistically definite value. The desquamating cases displayed a lower observed incidence of myocarditis than the control cases. This is probably due to the limited period of observation for most of the desquamators. In a group of 107 patients in which the scarlet fever was complicated by the presence of other infectious diseases no definite difference as compared with the rest of the material could be established.

Penicillin is apparently able to reduce the incidence of "severe" electrocardiographic changes in scarlet fever, although it shows only a tendency to reduce the actual incidence of myocarditis in association with the disease. Of course these observations and conclusions are valid only in milder epidemics of the sort seen in recent years. Should a severer type appear, penicillin therapy would in all likelihood assume a greater importance with regard to myocarditis in both adults and children.

In view of the present findings regarding the incidence of myocarditis, early penicillin treatment should be instituted in adults. With regard to myocarditis in children, it would seem that with infections of the current mild type treatment may be omitted or delayed. This is of practical importance in regard to the tendency to development of recurrences following early treatment of scarlatina with penicillin.

FROM THE AUTHOR'S SUMMARY.

THE ROLE OF NON-ANTIGEN INJECTIONS IN THE PRECIPITATION OF PARALYTIC POLIOMYELITIS. ANDERS HAGSTROMER, Svenska läk.-tidning. **50**:2692 (Dec. 18) 1953.

A critical review is given of the literature including investigations by Rosen and co-workers and Korns and co-workers. The former group's report on the Tahiti epidemic of 1951 is of special interest. A remarkable association between intramuscular injection (of diethylamine acetarsone [Acetylarsan], bismuth subsalicylate and/or mercuric iodide) and later onset of paralytic poliomyelitis was evident.

It seems possible that the injections had actually precipitated paralysis, though this can't be regarded as definite. This hypothesis can hardly explain certain interesting traits of the epidemic in that part of Tahiti (East Tahiti) where injections had been given so freely, i. e. (1) the high attack rate among the noninjected population of East Tahiti in comparison with the total population of West Tahiti; (2) the high relative attack rate among the noninjected contemporaries in age of those injected most.

Other influencing factors must therefore be questioned.

Rosen and co-workers did not rule out possible contagion risks in the doctor's reception room, i. e., indirect contagion from polio patients, contagion from virus carriers among the medical personnel, etc. Such possible contagion fits in well with all available evidence of the epidemic.

The association between penicillin injection and paralysis found by Korns and co-workers is not conclusive either. The localization of the paralysis in the inoculated limb was not convincing. Further, their two comparison materials were inadequate.

AUTHOR'S SUMMARY.

WATERHOUSE-FRIDERICHSEN SYNDROME. C. SMEENK, Maandschr. kindergeneesk. **22**:286 (Sept.) 1952.

Smeenk describes the case of a six-month-old baby with Waterhouse-Friderichsen syndrome caused by a meningococcal sepsis. The child recovered from shock following treatment with corticotropin (ACTH).

FROM THE AUTHOR'S SUMMARY.

THE TREATMENT OF PINWORM (ENTEROBIUS VERMICULARIS) INFECTION WITH BACITRACIN AND SULFASUXIDINE. K. F. CHAN and H. W. BROWN, J. Pediat. **43**:290 (Sept.) 1953.

Seventeen patients with Enterobius infection were treated with a combination of bacitracin and succinylsulfathiazole (Sulfasuxidine). The doses for adults was 120,000 units of bacitracin daily, in four doses, for seven days and 3 gm. of succinylsulfathiazole daily, in four doses, for seven days. The dosage for children was 10,000 units of bacitracin per 10 lb. (4.5 kg.) of body weight daily, in three or four doses, for seven days and 250 mg. of succinylsulfathiazole per 10 lb. of body weight daily, in three or four doses, for seven days. The criteria of cure were based on the evidence of six or more consecutive swabs negative for Enterobius eggs. On this basis, 91% of the patients treated in this manner were cured.

The authors mention that the appearance of Enterobius eggs in swabs after the third week may not indicate failure of treatment, as reinfection may become evident at this time.

MACDONALD, Pittsburgh.

CURRENT STATUS OF ACUTE RHEUMATIC FEVER IN THE STATE OF WASHINGTON. ROBERT A. BRUCE, Northwest Med. **52**:636 (Aug.) 1953.

The author presents a statistical survey of 1,200 replies received from the physicians of the State of Washington. The replies were to a questionnaire relative to the number of cases of rheumatic fever diagnosed by these physicians during the period from May, 1951, through June, 1952. There were 368 cases diagnosed as acute rheumatic fever. The statistics presented analyze the family histories, incidence of previous attacks, geographical distribution, and clinical characteristics of these patients.

The article continues with a comparison of these statistics with those of Bland and Jones, covering a 20-year period and 1,000 patients followed in Boston.

DOCTER, Seattle.

THE SYNDROME OF DIMINISHED SUSCEPTIBILITY TO ANTIMONY IN VISCERAL LEISHMANIASIS IN CHILDREN. J. BAX BARRIO and V. SANCHO PASQUAN, Rev. españ. pediat. **9**:4 (Jan.-Feb.) 1953.

The authors say that the term antimony-resistant should be replaced by the term "reduced susceptibility" to antimony. In defense of this idea they analyzed 51 cases of children with visceral leishmaniasis and found that, in children where the disease was long-standing or complicated by other conditions, antimony products were less effective or totally ineffective. In 96% of the total cases, antimony was effective; in the other 4% the pseudonephrotic, pseudoathreptic, and children with cirrhosis showed diminished response to the drug. In tertiary leishmaniasis there was a diminished response, and in one case each of tuberculous meningitis, hepatitis, and nephritis there was also diminished response, but they finally obtained recovery in a high percentage of all of these resistant cases, since only two died.

ALLEN, Santa Fe, N. Mex.

OXYURIASIS. JOAQUIN PASCUAL GISPERT, Rev. cubana Pediat. **25**:73 (Feb.) 1953.

Of 1,768 children from the province of Matanzas studied by microscopic examination of the stools, 69% had some parasite and 31% did not. In the positive cases, the following percentages of various parasites were found: Trichuris trichiura 50%; Giardia lamblia 13.01%; Ascaris lumbricoides 12%; Necator americanus 2.5%; Enterobius vermicularis 0.7%; Endameba histolytica 0.2%; and Taenia saginata 0.05%. However, on examination of 74 children by the cellophane-tape method of Graham, 23% were found to be positive for Enterobius vermicularis.

The author reviews the morphology and epidemiology of Enterobius vermicularis and the symptoms, diagnosis, and treatment of infection with this parasite.

NELSON, San Francisco.

GIARDIA LAMBLIA. MIGUEL A. BEATO, JUAN FLOR JORGANES, GUILLERMO CABALLERO, LAUDELINO H. GONZALEZ, and FELIX BURES, Rev. cubana pediat. **25**:88 (Feb.) 1953.

A complete review is given of the history, morphology, and epidemiology of this parasite, as well as the symptomatology and treatment of Giardia infection. The authors report on the incidence of Giardia infestation in Cuba.

A cure rate of 87.4% with one course of treatment with quinacrine (Atabrine) is reported. However, the authors do not state the number of stools examined or the length of follow-up in their criteria for cure.

NELSON, San Francisco.

AMEBIASIS WITH HEPATIC ABSCESS, DIAPHRAGMITIS AND PLEUROPNEUMONITIS OF THE SAME PARASITIC ORIGIN: CONDENSED CLINICAL REPORT. Bol. med. hosp. inf. **10**:185 (April) 1953.

The author presents a case of amebic ulcerative enterocolitis in a very malnourished one-year-old baby girl. It became complicated with hepatic abscess, diaphragmitis, and pleuropneumonitis of the same parasitic origin, aside from intestinal perforation followed by peritonitis; this last issue brought about shock. As a practical teaching in this case, comments are made on the convenience to keep always in mind the possibility of deceitful amebic pictures so frequent in Mexico in those cases of infectious diarrheas.

FROM THE AUTHOR'S SUMMARY.

RHEUMATIC FEVER IN A SIXTEEN-MONTH-OLD GIRL. A. SEBEK, Pediat. listy **7**:226, 1952.

Recent rheumatic endocarditis was found in a baby girl aged 16 months. Rheumatic verrucae were present on the tricuspid valve and on the endocardium of the left auricle; involvement of the other valves could be proved microscopically only. There were very few Aschoff's nodules in the myocardium. Death was due to dilatation of the heart and edema of the lungs. The young age of the patient is very exceptional; only 16 cases of rheumatic heart disease in infants under 2 years of age have been recorded so far.

FROM THE AUTHOR'S SUMMARY.

THE PREVENTION OF INFLUENZA IN INFANTS BY ANTI-INFLUENZAL INOCULATION OF MOTHERS. J. STRAUSS, B. STYK, B. TUMOVA, and L. ZEMAN, Pediat. listy **8**:34 (June) 1953.

Thirty-one women in their seventh and eighth months of pregnancy and 10 mothers in their first week after labor were subcutaneously inoculated with freshly prepared anti-influenza vaccine. The level of specific antibodies (hemagglutinin-inhibitory and virus-neutralizing ones) were then studied in both mothers and children in the second and third month after birth. For a period of six months after birth the sickness rate of mothers and children with reference to respiratory infection was followed. Out of the four antigens used in the preparation of the vaccine, the standard laboratory strains in the influenza virus (Type A PR 8 and Type B Lee) proved the strongest in antibody formation. Local strains of the influenza virus (Type A Cs 1 and Type B Cs 1) showed weaker antigenic qualities. Seven weeks after inoculation antibodies in inoculated persons increased on an average two-and-one-half- to five-fold. The titer of the virus neutralizing antibodies was, as a rule, lower than the titer of the hemagglutinin-inhibitory ones, but the movement of the levels with both methods were in agreement. The antibody titer of the umbilical blood in infants of inoculated mothers was twice as high as that in infants of the control group. The inoculation of mothers affected the level of antibodies in their children only for the first two to three months after birth. Towards the end of the third month the average level of antibodies was already low (1:32 to 1:128) and in keeping with findings in the control group.

The frequency of upper respiratory inflammations in the children of inoculated mothers was half that in children of the control group. Active immunization of mothers against influenza acts in the prevention of infection in infants in two ways: (*a*) diaplacental passage of antibodies, the significance of which is confined to the first months of life, and (*b*) by raising the resistance of the mother it eliminates from the infants' environment one of the common sources of influenza infection.

FROM THE AUTHORS' SUMMARY.

SUBSEPSIS ALLERGICA WISSLER. LARS GARBY, Acta pædiat. **82**:351 (July) 1953.

A description of three cases of Wissler's allergic subsepsis is given. No evidence of etiology and pathogenesis could be obtained. The close relationship to rheumatic fever and rheumatoid arthritis was confirmed. The beneficial effect of corticotropin (ACTH) is pointed out.

FROM THE AUTHOR'S SUMMARY.

A CASE OF CAT SCRATCH DISEASE. J. L. KEYZER, Maanschr. kindergeneesk. **21**:341 (Oct.) 1953.

Histological examination of a cervical lymph node removed from a 6-year-old boy was suggestive of tuberculosis as well as of blastomycosis. Clinical examination disclosed nothing abnormal, except for an increased erythrocyte sedimentation rate. Serum reactions for syphilis were negative. Tuberculin tests were also negative.

The possibility of benign inoculation lymphoreticulosis was suggested by the pathologist. The Mollaret test appeared to be strongly positive. The microscopic appearance was typical of the disease, as is illustrated by some photomicrographs. Nothing is known of a primary lesion in this case; some contact with cats, however, is certain.

FROM THE AUTHOR'S SUMMARY.

Chronic Infectious Diseases

A FIVE-YEAR STUDY OF TUBERCULOUS CHILDREN TREATED WITH STREPTOMYCIN. E. T. MCENERY, J. A. M. A. **153**:627 (Oct. 17) 1953.

Progressive primary tuberculous lesions in children responded well to streptomycin therapy during the first year and were well five years afterwards. In the adult type in children, on the other hand, after early vigorous treatment, including rest, pneumoperitoneum, and surgery, there remained much to be desired.

KIMBALL, Evanston, Ill.

EFFECTS OF RUBEOLA ON TUBERCULOSIS. A. V. MASCIA, F. E. CHICK, and W. E. LEVY, J. Pediat. **43**:294 (Sept.) 1953.

Rubeola had no effect on the primary tuberculosis of 13 children observed in this study.

MACDONALD, Pittsburgh.

THE CURE OF TUBERCULOSIS BY ALTERNATING DOSES OF STREPTOMYCIN AND OF THE HYDRAZIDE OF ISONICOTINIC ACID. G. SALVIOLI, Clin. pediat. **35**:131 (March) 1953.

The present routine treatment of patients with tuberculous meningitis at the Centro di Bologna involves the alternate use of streptomycin and the hydrazide of isonicotinic acid. For the first 90 days intrathecal treatments are of streptomycin; then for 30 days the hydrazide of isonicotinic acid is given intrathecally; thereafter, the drugs are alternated every 30 days. Streptomycin is given intramuscularly for the first 150 days and thereafter only in the periods when it is given intrathecally. The hydrazide of isonicotinic acid is first given orally on the 45th day of the treatment and continued for 30 days; thereafter it is given orally on the same days that it is given intrathecally. The clinical results of this new scheme of therapy have been better than under previous routines. The death rate has fallen from about 25% to about 15%.

HIGGINS, Boston.

THE DIFFUSION OF ISONIAZIDE, GIVEN INTRATHECALLY, IN COMPLETE SPINAL FLUID BLOCK IN PATIENTS WITH TUBERCULOUS MENINGITIS. M. ORLANDELLI and A. DEGLI ESPOSTI, Clin. Pediat. **35**:335 (May) 1953.

Twenty milligrams of the hydrazide of isonicotinic acid were given by lumbar puncture to each of eight patients, all of whom had a complete spinal fluid block in the course of tuberculous meningitis. In each case some of the drug was found in fluid obtained by cisternal puncture three hours later.

HIGGINS, Boston.

A CASE OF SUBACUTE TOXOPLASMOSIS DEVELOPMENT TO CHRONICITY. BERNARDO PEREZ MORENO, Acta pediat. españ. **11**:375 (June) 1953.

The author presents this case of toxoplasmosis in a child 6 years of age. It was the meningoencephalitic type and was apparently acquired at the age of 6 years, since no symptoms had been present until that age. The infection was from fleas on a family dog. There were four stages of development: (1) mild encephalitis, (2) remission with a complicating pneumonitis, (3) acute meningoencephalitis with chorioretinitis and blindness, (4) clinically silent period in which all symptoms disappeared but serious alterations persisted in the spinal fluid. Full reports of laboratory findings and the skull x-rays showing areas of calcification are included, as well as a detailed description of clinical symptoms.

Chlortetracycline (Aureomycin) was the only antibiotic which proved valuable. Intradermal reaction showed all members of the family strongly positive except the sick child, which shows the extent to which the disease may be latent in the population of Spain.

ALLEN, Santa Fe, N. Mex.

THE DANDY TEST IN TUBERCULOUS MENINGITIS. HUGO RESTREPTO HORTA and MARIANO LATORRE, Rev. chilena pediat. **24**:224 (July) 1953.

The different factors that have been suggested as prognostic indexes in tuberculous meningitis are analyzed, and the Dandy test is proposed as a new index to obtain an early knowledge of the absorption derangements so frequent during the course of this disease. The tests were done on 20 children with tuberculous meningitis, on whom also, to eliminate possible error, intravenous tests were simultaneously carried out. The results obtained indicate a clear-cut difference in elimination in those cases with good or bad prognosis.

In three cases Dandy's absorption index was not strictly parallel to the clinical progress, but these were classified due to the length of the treatment as chronic meningitis.

FROM THE AUTHORS' SUMMARY.

BCG Vaccination, Application of BCG, and Therapy with BCG in Pediatric Practice. Pedro Domingo, Rev. cubana pediat. **25**:137 (March) 1953.

The author points out the difference in meaning and use of BCG vaccine for vaccination in the person known to be tuberculin negative and in whom there is no possibility of contact with virulent organisms during the evolution of the BCG reactions, as contrasted with the patient in whom such contact may have occurred. The other use of BCG vaccine is for therapy in the person known to have been infected with virulent organisms. The author points out that clarification of the different uses of BCG will reduce the confusion that exists in this respect.

The techniques used and the results obtained with BCG are discussed in great detail. A discussion of the use of tuberculin testing followed up with BCG vaccination in a group of school children is excellent. This is a very good article discussing the logical uses of BCG. The author is the director of the "Instituto de BCG" of Havana.

Nelson, San Francisco.

Present Results of Occlusive Treatment of Meningitis Tuberculosa with Neoteben. Marianne Groll-Kahl, Deutsche med. Wchnschr. **78**:1270 (Sept. 11) 1953.

Isoniazid (Neoteben) was given by mouth and intraspinally to 21 children with proved tuberculous meningitis. Of these, four were admitted moribund. They died within three days. Fifteen survived an observation period of 3 weeks to 14 months. On the whole, the exclusive treatment with isoniazid has so far proved satisfactory.

Amberg, Rochester, Minn.

Diseases of Blood, Heart and Blood Vessels, and Spleen

Bone Marrow Aspiration Sites in Infants and Children. F. E. Schaar, J. Pediat. **43**:297 (Sept.) 1953.

Although the sternum is suitable for bone marrow aspiration in a cooperative patient, when the patient is apprehensive Schaar suggests that the ilium or tibia may be used. The author prefers the tibia in the newborn infant and in children under 2 years of age.

Macdonald, Pittsburgh.

Sickle-Cell Anemia with Unusual Bone Changes. R. E. Ivy and F. H. Howard, J. Pediat. **43**:312 (Sept.) 1953.

Ivy and Howard report an infant with sickle-cell anemia who had swelling of the hands and fingers. X-rays of the hand showed areas of radiolucency in distal metaphyses of the radius and ulna as well as in the metacarpals and phalanges. These were both subperiosteal and intramedullary. There was evidence of expansion of the bone but no evidence of newborn formation. X-rays of other long bones, chest, skull, and feet were normal. These symptoms are not frequently mentioned in descriptions of sickle-cell anemia, but they are probably not extremely rare. The pathogenesis is not clear. In this case, the osseous lesions disappeared in six months.

Macdonald, Pittsburgh.

A Case of Rheumatic Pancarditis, Treated and Cured by ACTH. G. Aceto, Clin. pediat. **35**:357 (May) 1953.

A 10-year-old boy with pancarditis responded quickly and well to treatment by corticotropin (ACTH) and cortisone.

Higgins, Boston.

Systemic Xanthomatous Granulomatous Reticulo-Endotheliosis, with Multiple Localization in the Lymph Glands and the Bones. M. Orlandelli and M. A. Dina, Clin. pediat. **35**:375 (June) 1953.

A well-nourished 6-year-old boy developed occasional attacks of fever and enlarged lymph nodes, especially the submaxillary and lateral cervical nodes, and spleen. He also had painful red swellings over some of the bones of the wrists, hands, and fingers. The blood cholesterol was 181 mg. per 100 cc. A biopsy of a lymph node revealed many reticulohistiocytes containing

various amounts of lipid material of varying chemical composition. X-ray films of the involved bones revealed rounded areas of decalcification. A diagnosis of Hand-Schüller-Christian disease seems to be ruled out because of the normal blood cholesterol and the absence of many other features of that syndrome.

HIGGINS, Boston.

ANOTHER CASE IN A CHILD OF THE WOLFF-PARKINSON-WHITE SYNDROME (PAROXYSMAL TACHYCARDIA). R. BULGARELLI and F. ABBO, Minerva pediat. **5**:650 (Aug. 15) 1953.

This is the second case of paroxysmal tachycardia in a child reported by the author (abstracted, A. M. A. AM. J. DIS. CHILD. **83**:220 [Feb.] 1952). The present patient, a 5-year-old girl, had at least nine severe attacks, three of them starting while she was in the hospital. In the severer attacks there were vomiting, pallor, cardiac enlargement, precordial pain, and enlargement of the liver. After a lengthy discussion of the pharmacodynamic aspects of the drugs available for treatment, the conclusion is reached that quinidine is indicated and digitalis is contraindicated in the treatment of paroxysmal tachycardia.

HIGGINS, Boston.

ISOLATION OF A MICRO-ORGANISM OF THE PLEUROPNEUMONIA GROUP IN PATIENTS WITH SCHOENLEIN-HENOCH'S PURPURA. J. MENEGHELLO, M. RODRÍGUEZ, O. UNDURRAGA, and R. BURDACH, Rev. chilena pediat. **24**:228 (July) 1953.

The authors describe three cases of Schoenlein-Henoch purpura in which an organism of the pleuropneumonia group was isolated. A detailed bacteriological study is presented. The pathogenic role of this bacterium is discussed.

FROM THE AUTHORS' SUMMARY.

A CASE OF PLANT-CELL EMBOLI IN THE CORONARY VASCULAR SYSTEM. F. BAJARDI, Wien. klin. Wchnschr. **65**:815 (Sept. 18) 1953.

A 12-year-old boy had repeated hematemesis and died 10 days after onset of symptoms. At autopsy a hemorrhagic exudate was found in the right pleural cavity. Purulent peritonitis and abscesses in liver, spleen, and kidneys were found. There was ulceration of the esophagus with perforation in the left atrium with lesions in the endocardium and in the adjoining intima of the aorta. In a section taken from the posterior wall of the left ventricle, a small artery was encountered filled mainly with a foreign body and to a lesser extent with a thrombus. The foreign body consisted of plant cells which had found their way through the perforation in the esophagus into the left atrium, the left ventricle, and so into the right coronary artery. The plant cells were found in other small arteries of the left posterior myocardium.

AMBERG, Rochester, Minn.

Diseases of Nose, Throat, and Ear

PROBLEM OF ACUTE LARYNGOTRACHEOBRONCHITIS. A. R. EVERETT, Eye, Ear, Nose & Throat Month. **32**:142 (March) 1953.

From 1942 to 1951, one thousand forty-five patients with laryngotracheobronchitis were treated on the croup service at Willard Hospital in New York. In this series there were 12 deaths, a mortality rate of 1.2%. This was a decided decrease from the 9% of the previous decade.

Laryngotracheobronchitis with obstruction is essentially a disease of infancy and early childhood. The administration of antibiotics and chemotherapy in the early stages of the disease has prevented the development of serious obstructive problems in many instances. If the respiratory effort is only slight, the patient should be kept quiet and comfortable in a cubicle, oxygen tent, or croupette, preferably with cool humidified oxygen. If, however, it appears that conservative procedures are not likely to prove successful, operative treatment should be instituted without loss of time.

Suprasternal, supraclavicular, intercostal, and epigastric retractions are positive signs of obstruction of the upper air passage. If the general condition becomes worse or if there is any evidence of increased respiratory obstruction and fatigue, intervention should be prompt or

the child will rapidly exhaust himself. Direct laryngoscopy should be done if tracheotomy is contemplated and suction equipment and airway are readily available. This will afford the opportunity to clean the trachea and upper bronchi of troublesome secretions. If the decision is made to do a tracheotomy, as is more than likely at this stage, an airway or small bronchoscope should be left in place during the operation. With the life-saving tube in place, the immediate emergency has been met, and the tracheotomy can be carried out in an unhurried manner. The presence of an airway of this type should be mandatory in patients with severe, acute obstructive symptoms.

The tracheotomized patient must be constantly attended by a special nurse, who is instructed to keep the trachea and upper bronchi clear of secretions by frequent aspirations with a small, soft rubber catheter through the tracheotomy tube. Room air and especially oxygen have a very drying effect upon the lower air passages when shunted through a tracheotomy tube. A plan for humidification, preferably mechanical vapor, must be instituted. This prevents irritation of the trachea and bronchi and crust formation. The addition of a wetting agent in the water to be vaporized may prove helpful in preventing crusting and in lessening the viscosity of the secretions. Antibacterial agents are routinely continued in appropriate doses postoperatively to prevent pneumonia and to control the original infection.

JENNES, Waterbury, Conn. [A. M. A. ARCH. OTOLARYNG.].

CONGENITAL ATRESIA OF THE NASAL CHOANAE. J. E. JOHNSON, J. M. A. Alabama **21**:357 (June) 1952.

Johnson emphasizes that atresia of the choanae should always be looked for in all cases of nasal obstruction. His custom is to examine each new patient with the electric pharyngoscope. Closure following operation is not uncommon due to contraction of scar tissue, the foreign-body effect of packing material or the obturators used. Of the various techniques for correction of this condition, Johnson chose the Owens method for its suitability in this particular case. The patient, a 26-year-old woman, had never been able to breathe through her nose; mouth breathing had not caused hearing impairment or sinus trouble. There was congenital defect in the eyes. In the nose there was relative hypertrophy of all the turbinates, with slight left deflection of the septum. The palatal arch was excessively high, with a prominent bony ridge the entire length of the hard palate. At operation it was found that this condition was due to the unusual downward growth of the bony nasal septum. The x-ray, with a radiopaque marker, revealed extreme narrowing of the posterior extremity of both nostrils. On incision the occluding membrane was found to be very fibrous and resistant. After removal of the membrane the margins were closed with black nonabsorbable (silk) surgical sutures extending through the periosteum. No obturators or packing were employed. Douches of an isotonic sodium chloride solution were used on the first post-operative day and continued the following day when the patient was discharged. No later complications arose, and there has been no evidence of secondary choanal closure. Details of the operation are fully described.

SELTZER, Philadelphia [A. M. A. ARCH. OTOLARYNG.].

A PICTURE-TYPE SPEECH SOUND DISCRIMINATION TEST. WILBERT PRONOVOST and CHARLES DUMBLETON, J. Speech & Hearing Disorders **18**:258 (Sept.) 1953.

The Mansur picture-type test of speech-sound discrimination was revised by the authors to avoid some of the deficiencies of the original test and administered to 434 first-grade children. The instrument is valid and reliable but subject to some limitations. It does not test on a high enough level of speech-sound discrimination to be used in a definitive study of the normal population. When used as a diagnostic instrument it is valuable as an indicator of the adequacy of a child's speech-sound discrimination ability. A limit on the validity of the instrument individually used is the articulation of the person administering the test. A tape-recorded test would be more valid if used under controlled acoustical conditions.

PALMER, Wichita, Kan.

News and Comment

Twenty-Second Annual Series of Benjamin Knox Rachford Lectures.—Charles H. Rammelkamp, M.D., Professor of Medicine at Western Reserve University School of Medicine, Cleveland, will deliver the 22d annual series of the Benjamin Knox Rachford Lectures on Thursday evening, Feb. 25, and Friday evening, Feb. 26, 1954, at 8:30 p.m. in the auditorium of the Children's Hospital Clinic and Research Building, Cincinnati. The titles of his lectures are (1) "Acute Streptococcal Infections and Rheumatic Fever" and (2) "Acute Hemorrhagic Glomerulonephritis."

Books

Physiological Foundations of Neurology and Psychiatry. By Ernst Gellhorn, M.D., Ph.D. Price, $8.50. Pp. 556. University of Minnesota Press, Minneapolis 14, 1953.

This book is, in the main, a review and integration of neurophysiology in the last 15 or 20 years. The work of the author is the backbone onto which is grafted the work of others doing research in this field. The bibliography consists of 53 pages and 1,263 references. The extensive and intensive nature of this work can be judged not only by the enormous bibliography, but also by the divisions into parts. There are six parts: Intrinsic and Extrinsic Factors Regulating Neural Activity, Contributions to the Physiology and Pathology of Movements, The Physiological Basis of Consciousness, Some Aspects of Autonomic Physiology, Integration, and, lastly, Applications.

A great deal of experimental work is brought into line with clinical experience, and in this respect certain sections will be of interest to the medical profession at large. Neurolgists, neurological surgeons, and psychiatrists will find this a useful reference book dealing with the advanced work which may eventually broaden their own horizon. The part on the physiology and pathology of consciousness is a matter of interest to all. The physiological basis of emotion has a practical application which will be stimulating to psychiatrists.

Part 6 of the book deals with the application of this mass of maternal to clinical psychiatry, and in it are taken up the basis of shock therapy, carbon dioxide therapy, and the analysis of autonomic tests in the psychoses.

It appears, however, that this volume may find its principle value as an inspiration and a book of reference for those working in the field of experimental neurophysiology. There is extraordinary attention to detail and a vast amount of careful thought involved in retaining and piecing together the extensive material used. The labor in putting the material together could not be done without sustained and concentrated effort. The author's own experimental work is certainly brought to the fore in most of the subject matter, but this is to be expected from one who has worked so continuously in the field. The reviewer read the book from cover to cover, and, although he was not always able to follow with complete clarity, he received a great stimulus from the experience.

The book fills a very great need in the field of neurological science offering an authoritative and informative integration of neurophysiological research and its present application to the clinical field. It is recommended to all those who wish to learn some of the practical applications of the vast amount of work that is being done in neurophysiology.

Microbiology and Human Progress. By Madeleine Parker Grant. Price, $6.75. Pp. 718, with 29 illustrations. Rinehart & Co., Inc., 232 Madison Ave., New York 16, 1953.

To quote from the author, "This college text was written for introductory courses in bacteriology and microbiology, particularly for students whose major interests lie outside the field of science." In order to do this the author has used some of the subject matter of microbiology to illustrate certain broad concepts pertaining to life in general and human life specifically. Much

material is utilized to illustrate the scientific method of biology, the implications of microbiology from an evolutionary point of view, and its relationship to hypothesis concerning the origin of life. In the second part of the book the microbes are considered in all those situations where these, by their existence, benefit man, such as their role in nitrogen fixation, fermentative food processes, antibiotic production, and many others. In the third part the pathogenic organisms are considered in some detail, as well as the defense mechanisms which protect man from the micro-organisms.

In that this book is designed for readers who may have had little or no previous science training, there are well-written sections giving simplified outlines of such subjects as atomic structure of matter, animal and plant genetics, physics of the light and electron microscopes, and similar pertinent information. It is the reviewer's opinion that an approach of this type should make a valuable course for the student who is not going to pursue a bacteriologic or scientific career, just as an informative literature, history, or similar course will greatly benefit a student who ultimately pursues a scientific specialty.

In trying to achieve this aim the book is probably not too suitable for a first course in bacteriology for a student expecting to specialize in the field, since a more comprehensive and detailed learning process would seem in order. There are many pages, however, which could serve as the starting point of a seminar for the more advanced bacteriology student.

It is difficult to predict how well the book will achieve its goal. In spite of masterful simplification of some complex fields, there are many sections in which the vocabulary and concepts would appear to be too complex for a student without a rather good background or much supplemental explanation. The choice of material to use as the illustrative basis must have given the author a considerable problem. As in all situations where there is a wealth of data from which to choose, the reasons for some of the choices seem obscure. It is felt by the reviewer, for example, that perhaps there is too much emphasis on certain pathologic processes for a course of this type. This is particularly impressive to one who has had experience with the difficulties that medical students, who are infinitely better prepared, frequently experience in adjusting to the description of disease.

The use of figures is excellent, particularly in that the legend is clear, explanatory, and well related to the text. Detailed study of the figures and legend will give much of the attitude which the author intends to impart. The chapter entitled "The Meaning of Health," which embodies the modern concepts of preventive medicine, is extremely well done.

It would be exciting and interesting to teach a course to the students for whom the book is intended, using it as a text.

Le Pneumopatie Infettive del Feto e del Neonato. By Giuseppe Valle. Price, 2,500 lire. Pp. 231, with 54 illustrations and 12 tables. Edizioni Minerva medica, Via Martiri della Libertà, 15, Torino, 1953.

The author uses the pathological-physiological approach to the subject of pulmonary disease in the fetus and the newborn. The prenatal, the intranatal, and the postnatal periods are considered in turn, the pathology and physiology in each affording the basis for therapeutic and prophylactic approach. The illustrations are well prepared and the photographs clear and well chosen. A bibliography of about 500 references is given. The book illustrates well the dictum that when what is going on in a diseased state is well expressed, therapeutic procedures become obvious. The author is to be commended on a job well done.

Chronic Pulmonary Emphysema Physiopathology and Treatment. Modern Medical Monograph Series. By Maurice S. Segal and M. J. Dulfano. Price, $5.50. Pp. 180, with 31 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1953.

The pathology, physiology and treatment of chronic pulmonary emphysema are discussed in the light of their clinical manifestations in this authoritative monograph. Particularly well covered are pulmonary function tests and the carbon dioxide intoxication syndrome. Emphysematous patients characteristically have decreased vital capacity, increased residual air volume, and diminished ventilatory reserve. Hypoxia is present even at rest in the later stages of the disease, and respiratory acidosis occurs in the final stage. The latter is established by simultaneous pCO_2 and pH determinations on arterial blood and is characterized by increased partial

pressure of CO_2 in the presence of a lowered pH. The effects of respiratory depression, by either depressant drugs or overzealous oxygen therapy, are emphasized. Sections on management are up to date and applicable to general clinical practice. Included are discussions of oxygen therapy, cortisone and corticotropin, aerosols, mechanical breathing apparatuses, and pneumoperitoneum.

This monograph is readable and pertinent. The illustrations, paper, and type are of good quality, but the binding is inadequate. The book will be useful to the internist and general practitioner, but will be of limited value to the pediatrician.

Improving the Child's Speech. By Virgil A. Anderson. Price, $5.50. Pp. 333. Oxford University Press, Amen House, Warwick Sq., London, E.C. 4; Agent for U. S. A., 114 5th Ave., New York 11, 1953.

Many of the speech and hearing disorders most frequently seen in the public schools are summarized to provide classroom teachers with elementary information concerning these defects. Such information is needed by school teachers, but because of the limitations of the audience in regard to basic information in physiology, psychology, medicine, and similar disciplines, the book contains only a superficial analysis of these speech disorders. Methods of correction are presented which are in the nature of selective techniques and may or may not produce the results desired. The medical problems presented by many of these cases are not covered, and the many neurological disorders which are involved in the production of speech and hearing handicaps are not discussed except in very brief form. The subjects covered are the nature and development of speech, the recognition of speech disabilities, the special problems of children with these handicaps, and general advice on integrating such training with the school curriculum.

Modern Concepts of Communicable Disease. By Morris Greenberg, M.D., and Anna V. Matz, R.N. Price, $6.20. Pp. 567. G. P. Putnam's Sons, 210 Madison Ave., New York 16, 1953.

In this book the authors give a clear and concise resumé of the communicable diseases from the epidemiologic point of view. As pointed out in the preface, the material was adapted in large part from a course on epidemiology for graduate students in a school of public health. From this point of view the choice of material and its presentation is more suitable for the allied professions than it is for the medical student or practicing physician. However, as a rapid refresher of the changing concepts, shifts in emphasis, and newer knowledge in the field, this book would be useful to the interested practitioner.

The book is divided into two parts. Part one concerns itself with the principle of communicable disease control. The discussions are brief, and many, such as the discussion of infection, resistance, and allergy, are designed to fill in possible gaps in preexisting knowledge of the nonphysician reader. The chapters on the care of the patients with communicable diseases in the general hospital, medical asepsis, and related topics are most pertinent to the every day problems confronting physician, nurse, and administration in the care of these patients. They are recommended to help answer pertinent problems which arise when such a patient needs hospitalization or home care.

Part 2 is a study of specific communicable diseases considered alphabetically under the general headings of respiratory diseases, food- and water-borne diseases, contact diseases, and diseases transmitted by arthropods. The discussion of each disease is brief but inclusive. The symptomatology and treatment aspects are not emphasized. Nursing care and techniques are given a prominent place. Several areas of treatment seem inadequately handled. For example, it is stated that "No specific treatment is available" for primary atypical pneumonia, without any discussion of the tetracycline drugs except to say that "Claims have been made for some antibiotics."

Similarly, no mention is made of the benefits of antibiotics in the treatment of acute streptococcal pharyngitis in the prevention of rheumatic fever. A few errors also are present such as the statement under the tuberculin test (page 279) that a positive reaction is indicated when there is an induration 5 cc. or more in diameter.

The book is easily read. It is a convenient size and has a simple format. There are but a few illustrations.

Health Saboteurs. By Robert William Davis, M.D. Price, $4. Pp. 306, with 47 illustrations. Pageant Press, 130 W. 42d St., New York, 1953.

The book is written to introduce the problem of tonsils and adenoids to patients and interested friends. It develops the thesis that many forms of crippling can be prevented by the removal of diseased tonsils and adenoids. Examples are the child with impaired hearing whose earning power and social activity will be curtailed, the girl with protruding teeth, the boy whose restricted airway prevents proper chest development, and the child with preventable heart, joint, or kidney disease.

The chapter on "Tonsils and Longevity" states that a clean throat prolongs life.

In the chapter on "Controversy regarding Tonsillectomy" the author states that "Better still than the recovery of normal function is the prevention of its (the tonsil) becoming deranged in the first place." The author wishes to go on record as advocating the removal of tonsils and adenoids at the age of 4, irrespective of condition, or even at the age of 2 or less. He states "The law of diminishing returns starts to operate at an early age. This is an age of sanitation and prophylaxis in medicine."

In the chapter on "Focal Infection" pathology is presented to demonstrate why the tonsil is potentially dangerous.

In the chapter on "Function of the Tonsils" the author traces biological development. The process of evolution is detailed to give a factual basis for minimizing tonsil function. The point is stressed that the tonsil being of late embryonic development failed to become enclosed in its capsule in contrast to the thymus and thyroid, which are encapsulated and remote from the throat surface. The statement is made that the tonsils and adenoids do not have a sufficiently important function at the present time to offset their deleterious effects. Various indications for tonsillectomy and adenoidectomy are outlined.

In the chapter on "Tonsils and Sinus Diseases" the statement that "Many authors point out that tonsillectomy will cure upward of 80% of cases of sinusitis" is definitely open to challenge.

The chapter on "Tonsils, Crooked Teeth, and Facial Deformities" is logical and informative.

The chapter on "Tonsils, Deafness, Ear and Mastoid Infections" is well presented quoting recognized authority.

The chapter presenting "Tonsils and Chest Deformities" is perhaps too briefly presented.

The chapter on "Tonsils, Climate, Health and Headshapes" presents a confused subject matter, much of which does not concern the immediate subject directly.

The chapter on "Rheumatic Fever" stresses the throat as the chief portal of entry of the infecting agent. There is no discussion of the use of antibiotics.

Nephritis is briefly mentioned as a secondary avoidable infection. The author states that "It behooves us until the true cause of hypertension is known to eliminate all sources of acute and chronic infection." Without presentation of evidence, the author suggests that diabetes might also be prevented by early tonsillectomy and adenoidectomy to prevent infections from curtailing the natural supply of hormone, that is, cortisone. The author believes that early tonsillectomies would tend to lower cancer incidence by hindering the development of irritating disease conditions. The author would prevent dental sepsis by the same method.

The chapter on "Tonsils and Industry" stressed the economic loss from diseased tonsils.

In the chapter on "Tonsils and Allergy" the controversy as to whether tonsillectomy and adenoidectomy accentuates the allergy is avoided.

The book presents the very radical view of the elimination of tonsils and adenoids, so the subject matter is very controversial. No seasoned otolaryngologist or seasoned pediatrician would adopt the policy of blanket removal of all tonsils and adenoids. The book ignores the development of the antibiotic age. It would not be considered a safe guide for the young trainee.

The Normal Child. By Ronald S. Illingworth. Price, $6. Pp. 342, with 63 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1953.

"The Normal Child" is devoted to the first three years of life. The book is divided into four sections, on feeding, physical, developmental, and behavior problems.

In compiling the book the author has used a good, practical, readable, and concise style. It is well organized and covers the important facets of child development without delving deeply

into the theoretical fields of medicine and psychiatry. No subject is covered to exhaustion, but no highlights are omitted. His information is current as evidenced by the inclusion of a chapter on accident prevention, a subject much emphasized in pediatrics today.

A book such as this may be of real value to a pediatrician or general practitioner who handles many infants, as a guide to what the normal child should do and how it should develop, because of its simplicity and organization. It would be a good book to have in a medical student's reference library.

Professor Illingworth has used a large number of references in writing the book which are listed for further reference if one wishes.

This book can very well be recommended as part of a young pediatrician's office library, as it might be referred to frequently in daily practice.

Office Management of Ocular Diseases. By W. F. Hughes Jr. Price, $9. Pp. 452, with 120 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 11, 1953.

Practical and precise details of diagnosis and treatment mark this comprehensive book on office ophthalmology. Basic science background is given so that one can appreciate why given methods are used. A remarkable amount of detail and broad "horse sense" knowledge of the whole field has been put together in one volume. Numerous drawings, tables, and photographs illustrate optics, lid surgery, diseases, injuries, etc.

The pediatrician will find an up-to-the-minute description of retrolental fibroplasia and will appreciate why immediate care for obstructed tear ducts and imbalances of the ocular muscles is so important. Thirty-one pages of formulary and exact details of drug usages is a very valuable section of this book. Extensive description of beta-ray and other radiation therapy with which the author has worked is given.

The ophthalmologist and pediatrician will each profit by a careful reading of this book. A small bibliography with each chapter makes further material easily available.

On the office shelf it will give the exact answers to most of the questions of dosage, exactly how to do it, etc.

Scientific Principles in Nursing. By M. Esther McClain, R.N. Edition 2. Price, $3.50. Pp. 409. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

This book presents a good over-all picture of the scientific principles of nursing. In this second edition the author has revised each chapter. It is not an exhaustive treatise, and the author has not attempted to describe techniques or to give procedure in detail; rather she shows us how the basic scientific principles may be applied to nursing. She points out that the sciences which relate to nursing are the physical, biological, medical, and social sciences, and in each chapter she has divided her discussion to cover these various phases. Of special interest were the suggested performance check lists. These would be valuable to the instructor, the head nurse, the staff teacher, and to the nurse herself. In using these lists, the nurse would be able to evaluate her performance and to see where she needs to place more emphasis on certain details. The chapter on public health is good, and the organization charts are excellent. Of particular interest and importance is the stress placed on nursing today, that it is a community service and every nurse is a teacher of health. In order for the nurse to be effectvie in her teaching, she must have a scientific background united with proper skills and attitudes.

Clinical Allergy. By French K. Hansel, M.D., M.S. Price, $17.50. Pp. 1005, with 84 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

This is a large comprehensive book. It is completely up to date and is an excellent and very thorough discussion of the present status of clinical allergy. It is written by a man who is primarily an otolaryngologist and who has probably devoted more time and thought to allergy of the upper respiratory tract than has anyone else. As might be expected, the section on allergy of the nose and paranasal sinuses, which comprises 161 pages, is the most valuable part of the book and is undoubtedly the best and most complete discussion to be found anywhere, as it reflects the large personal experience of the author.

There are very good and up-to-date chapters on the antihistamine drugs, on the use of cortisone and corticotropin (ACTH), and a section of 54 pages devoted to allergy in children. It is obvious that this section, with the exception of the portion on the nose and sinuses, is based more upon the experience of others than upon the author's own; the same may be said for the section on dermatologic allergy. These sections, and several others, are more in the nature of reviews than the author's own convictions and experiences. However, they are good reviews.

Dr. Hansel's method of immunization with pollen and other environmental allergens is well known, but not followed by the majority of allergists. It consists in the frequent injection, often intracutaneously, of very minute amounts of antigen, often as little as 0.05 cc. of a 1 : 10,000,000 dilution, very rarely as much as 0.10 cc. of 1 : 1,000. This he calls the "optimum dosage method." His treatment of hay fever is entirely coseasonal, and for the average patient with ragweed hay fever six to eight inoculations usually suffice. The proper dosage for each patient is determined by a titration of the skin sensitivity. Although he considers this method of treatment the best and uses no other, there is an adequate discussion of the more orthodox methods of treatment followed by most allergists.

Dr. Hansel highly recommends small doses of Staphylococcus toxoid in the treatment of all types of allergy, as well as for Staphylococcus infection. He says "Complete relief of itching (in atopic dermatitis) may be obtained by the use of small doses of Staphylococcus toxoid." This is indeed an extraordinary statement. However, nobody has a right to contradict it until he has himself tried the method. Dr. Hansel's statement that "injection therapy for various animal emanations, house dust, molds, pollens, etc. is usually effective" (in atopic dermatitis) is open to criticism. Many allergists and dermatologists who are upon intimate terms with atopic dermatitis are agreed that desensitization treatment, while it may occasionally produce good results, is on the whole not very satisfactory.

No man can write a book which does not contain material which will be criticized by any reviewer; there are plenty of things in this book which are contrary to this reviewer's experience and convictions. In spite of this, it is his opinion that Dr. Hansel has written an important and excellent book, which all those seriously interested in allergy will want, if only for the section on allergy of the nose, sinuses, and ear.

Pediatric Nursing. Edition 2. By Gladys S. Benz, R.N., B.S., M.A. Price, $5.25. Pp. 624, with 122 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

This book is intended for a text for student nurses. The author writes from a wide background of experience in pediatric nursing. The purpose of the book as stated in the preface is to (1) illustrate some of the reasons why each child must be treated as an individual—as a whole person with a definite place in the community; (2) beckon the student on to further exploration of the many facets of child care; (3) show how previous experience forms the foundation for pediatric nursing, and (4) suggest how the nurse as a person affects the care given.

The text is divided into five units: (1) The Development of Pediatrics, (2) The Newborn Infant, (3) Growth and Development, (4) Developing Skills in Nursing, and (5) Diseases Affecting the Body Systems. Ample annotated bibliographies are included at the end of each unit and some individual chapters. Illustrations are meaningful and well chosen.

For the most part, the author seems to have accomplished her purpose. The text is interesting, has current medical concepts, and treats common nursing problems in the care of children. The approach is from the normal to the abnormal, and needs for growth and development are considered for the child in health plus those imposed by his abnormality. Emphasis is placed on the individuality of the child as an integrating personality, influenced by the family and the community. Sociological considerations are adequate. Provision for optimum health as well as preventive aspects of disease are presented. The importance of desirable personal qualities of the nurse in caring for children is stressed.

Physical aspects of normal growth and development are discussed more extensively than the mental, emotional, and social aspects. The neonatal and infant periods are treated comprehensively. The preschool, school age, and adolescent periods are each delegated to a little more than one page, although material pertinent to these ages is scattered throughout the book. This presentation tends to delay the reader in the formation of the concept of the "whole child" at

these ages. The nutrition and eating habits of children above the age of infancy are discussed very briefly. Chapters on play and play equipment, the admission and discharge of a child from the hospital, and modern trends in child care are very well done. In the fifth unit, the more common conditions in children are stressed with comprehensive nursing care described. Many uncommon conditions are mentioned, and, in some instances the material is vague and meaningless.

This book is recommended as a modern text. Its value depends upon the level of the student who will be using it. For the basic three-year student, parts of the book seem presumptive of her psychological background. For the collegiate student, some of the material might seem elementary in its lack of detail, especially in disease conditions. All students and instructors will find the bibliographies helpful. "A Teachers' Guide for Pediatric Nursing" is available for use in conjunction with the text and has suggested methods of implementing the students' learning experiences.

Report of the Committee on Immunization and Therapeutic Procedures for Acute Infectious Diseases. By The American Academy of Pediatrics. Price, $0.50. Pp. 69. Evanston, Ill., 1952.

This familiar booklet has been revised since 1951 and changes made to incorporate differences in procedures that have become well established. Many public health agencies have accepted the academy's recommendations as standard. Wider acceptance would result in fewer obsolete practices, since the academy report is frequently revised.

This authoritative pamphlet is gaining more and more recognition and constitutes an extremely valuable aspect of the work of the academy. It is a most essential part of the library of every physician dealing with children.

Physician's Handbook. By Marcus A. Krupp, Norman J. Sweer, Ernest Jawetz, and Charles D. Armstrong. Price, $2.50. Pp. 380. Lange Medical Publications, University Medical Publishers, P. O. Box 1215, Los Altos, Calif., 1952.

This is the seventh edition of a popular handbook of information. It has been revised every two years since its inception, and in this edition has undergone extensive changes.

As a quick reference handbook, this is probably the most complete available. Everything from laboratory procedures to physical examination and history taking is included. There are sections on poisoning, radioisotopes, fluid and electrolyte balance, oxygen, carbon dioxide, and helium therapy, in fact on practically every special procedure or examination known. The book is a fund of readily available information and would be valuable to almost anyone practicing medicine.

Office Psychiatry, the Management of the Emotionally and Mentally Disturbed Patient. By Louis G. Moench, M.D. Price, $6. Pp. 310. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 1952.

The physician without special training in psychiatry finds himself in a dilemma when confronted with patients in whose disease psychic factors are prominent. If he attempts to treat the emotional aspects of his patients, he is apt to be criticized by the psychiatrist for his temerity in venturing into a field where his ignorance is liable to cause harm. If, on the other hand, he neglects to give attention to the psyche, he will be criticized for the narrowness of his attitude.

Within recent years a number of psychiatrists have come to appreciate that physicians, by and large, must of necessity be the ones to apply psychiatric knowledge. Moreover, experience has shown that they are, as a group, good psychotherapeutists.

In "Office Psychiatry," Moench has set out to present to the physician a clear, simple, and useful statement of modern psychiatric concepts. The author avoids the special jargon and obscure unsubstantiated concepts which have alienated the critical physician. Of special interest to the pediatrician are chapters on the growth and development of personality and on adolescence. The book makes easy, pleasant, and rewarding reading.

Cancer in Man. By S. Peller. Price, $12.50. Pp. 556, with no illustrations. International Universities Press, Inc., 227 W. 13th St., New York 11, 1952.

Dr. Peller must be congratulated on the scope of his endeavor and the excellence with which it has been executed. The epidemiological method of presentation has been most effectively utilized without the confusion of mathematical statistics.

The purpose of the book is to review contributions to the development of present cancer knowledge and theories, to discuss the philosophy of medical thinking in matters of cancer, to evaluate research of the past 50 years, and to analyze the discrepancies between achievements and expectations of cancer studies during this period.

The subject matter has been presented in three parts. The first of these contains a discussion of the cellular concept and its underlying philosophy and outstanding results of experimentation, with an evaluation of experimental trends. The second part pertains to the epidemiology of cancer. It is an extensive survey of cancer disposition in groups, as determined by biology, childhood, pathology, occupation, reproductive activity, sex hormones, and dermatropic influences.

Of particular interest is the chapter on childhood cancer, which includes recent unpublished studies by the author. Dr. Peller presents an interesting hypothesis for the transplacental exposure of the fetus to cancer-relevant substances, and concludes that about nine-tenths of childhood cancers are leukemias, sarcomas, mixed tumors, and gliomas, because nine-tenths of the tissues reached in the fetus over the umbilical cord are of either mesenchymatous or glial origin.

In the concluding chapters of this section, data are presented which convincingly suggest the possibility of acquired specific resistance to cancer. After a survey of 5,876 cancer cases, the author believes that a cured skin or lip cancer usually, but not always, prevents the growth and development of an internal primary tumor.

The third section of the book is devoted to the presentation of a new concept of cancer control and the indirect supporting measures required to make it effective. This concept states that, "Exposure of a population to carcinogenic agents which (*a*) provoke the development of tumors of a low case fatality ratio, and (*b*) are too weak to increase considerably the incidence of cancer carriers above the norm (that is approximately 20 per cent of all adults) will prevent the development of highly fatal tumors in other organs. The net result is bound to be a cancer mortality diminished by almost 90 per cent. The earlier in youth that exposure starts, the more effective will be the results." Although Dr. Peller has presented his unusual theories in a most provocative manner, there will undoubtedly be those who will not accept such theories on the basis of the facts contained in this book.

"Cancer in Man" provides a vast supply of stimulating information which should be interesting and valuable to all who are concerned with the problem of cancer. It is clearly presented and completely documented, including an author and a subject index.

Précis de Génétique Médicale. By Maurice Lamy. Price, 1,400 francs. Pp. 256, with 108 illustrations. Gaston Doin & Cie., 8 place de l'odéon, Paris, 6e, 1952.

This brief introduction to medical genetics was written by an outstanding French pediatrician who is now professor of medical genetics at the University of Paris. By this dual role, Dr. Lemy is unusually qualified to write a well-balanced account of medical genetic problems. The author commences with an explanation of the general principles and mechanisms which govern genetic transmission. Many good diagrams and well-chosen examples from human pathology illustrate this general section, which makes up about one third of the book. A later chapter deals with mutations and the origin of hereditary abnormal traits in man. In constrast to most textbooks of genetics, which avoid a thorough discussion of genetic and environmental interaction in the causation of diseases and anomalies, Lamy assigns a special chapter to this difficult and controversial subject. He emphasizes the important role which twin pathology plays in the distinction of genetic and environmental causes of human disorders. A large section deals with the heredity of pathological traits occurring in man. Although only small paragraphs are allotted to each disorder, the reader interested in a special subject can find references to original articles or monographs at the end of the book. The difficulties

of genetic prognosis and of eugenic measures are discussed. The last chapter deals with the elements of statistics and biometry. The book is well written and should be of practical value to physicians and medical students.

1952 Year Book of Pediatrics. Edited by Sydney S. Gellis, M.D. Price, $5.50. Pp. 423. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 1952.

The old familiar Year Book appears this year under a new editor, Dr. Sydney Gellis. In form and content the volume is unchanged. As before, it contains an excellent cross section of the pediatric literature of great value to all pediatricians as well as to any physician dealing with children.

Two changes are noteworthy. First is the somewhat more frequent and detailed editorial comment, which retains its instructive value. Second is the frequent use of comment on special problems by guest editors whose comments add considerably to the individual pages discussed, as well as providing an authoritative discussion probably not ordinarily obtained from the experience of a general editor.

Dr. Gellis is to be congratulated on his handling of his first edition of the Year Book.

Poliomyelitis: Papers and Discussions Presented at the Second International Poliomyelitis Conference. Compiled and edited for the International Poliomyelitis Congress. Price, $7.50. Pp. 555, with illustrations. J. B. Lippincott Company, 227-231 S. 6th St., Philadelphia 5, 1952.

The published report of the Second International Poliomyelitis Congress, as might be expected, reflects the increasing complexity of studies on this disease and the increasing importance of contributions from fundamental research in the solution of clinical problems. The conspicious emphasis on virology and immunology as well as on neurophysiology is in marked contrast to the relatively brief sections devoted to clinical aspects of poliomyelitis.

Formal presentations are grouped in Symposia and Reviews, in either case being followed by discussions. The latter, in most instances, represent short prepared talks on some aspects of the day's subject rather than spontaneous comment on preceeding papers. The roster not only of principal speakers but also of discussors includes most of the names familiar to students in this field.

A new and most attractive feature of the volume is approximately 150 pages devoted to excellent exhibits displayed at the congress. Charts, figures, and pictures, including some in color, are present in profusion, and brief descriptions by the exhibitors are succinct and well planned.

Neither symposia, reviews, nor exhibits reflect current interest in gamma globulin as a means of bestowing passive immunity. This seems odd until the time sequence of the congress with respect to passive immunization studies in this country is recalled.

The volume, then, is an important and authoritative reference, in addition to being a compilation of historically important opinions and documents. All physicians will find important information in the report, but many will also find detailed discussions on special problems of limited general interest. The job of publishing has been skillfully and richly done.

Franconi and Wallgren's Textbook of Pædiatrics. Edited by W. R. F. Collis. Price, $19.50. Pp. 1104, with 441 illustrations. Grune & Stratton, Inc., 381 4th Ave., New York 16, 1952.

This is the first new European pediatric text to appear since the war, having been published both in German and English. Dr. Franconi and Dr. Wallgren have enlisted the aid of colleagues from Switzerland and Sweden, as well as Holland, Finland, Norway, and Turkey. As the editors feel that the appeal of a European text to English-speaking pediatricians lies in its presentation of the views of the European pediatricians, this approach, rather than the presentation only of material which has stood the test of time, has been used.

In comparison with the more encyclopedic American texts, this book is brief. In most cases, the brevity is in its favor, little of importance being omitted. Syphilis, for example, covers 13

pages, as against 32 in the largest American text. Greater emphasis is laid on psychiatry, this section being very good. It includes the education of the normal child as well as mistakes made by the parents.

An interesting section is that on constitution, heredity and diatheses, the latter topic not usually being considered in this country. Sociological aspects of pediatrics are considered in greater detail than is ordinary in American books.

The opening chapter is on growth and development, which includes intrauterine development. This is followed by sociological aspects of pediatrics, examination of sick children, constitution, heredity, and diathesis, psychology of the normal and abnormal child, nutrition, with a consideration of the disorders of nutrition, and disorders of metabolism. Vitamins and vitamin deficiencies are also included. There are chapters on the newborn baby, prematurity, puberty, and adolescence, endocrinology, and infectious diseases. Diseases of the various organ systems, surgical conditions in childhood, diseases of childhood peculiar to hot climates, and care and feeding of the baby are also included. The final chapter is a synopsis of medical treatment.

This book is difficult to compare with American texts. Its approach is more clinical than most of ours and less coldly scientific. Despite this, it is not lacking in the newest developments of scientific medicine. Reading a section of Franconi and Wallgren is like attending a clinic by one of the great clinicians.

The presence of such names as Franconi, Wallgren, Liebesstein, Siwe, van Creveld, and Glanzmann is a sufficient index of the quality of the authors. The illustrations are excellent, and the book is handsomely bound and printed. It is well worth reading.

The Mentally Retarded Child: A Guide for Parents. By Abraham Levinson, M.D. Price, $2.75. Pp. 190, with 2 illustrations. John Day Company, Inc., 210 Madison Ave., New York 16, 1952.

This little book consisting of 190 pages in 18 chapters is written primarily for the parents of retarded children. The description of the anguish of the parents of the mentally retarded child is realistic. The advice to parents and the historical survey chapters are worth while. The vocational training discussions, especially the role of the parent, are first class. The discussion of treatment, however, is too optimistic and may convey false hope to the laity. The lists of schools and institutions throughout the country are convenient, although the tuition fees even now are out of date.

Physiological Changes in Plasma Proteins Characteristic of Human Reproduction: Cross-Sectional and Longitudinal Electrophoretic Data for Women During and Following Uncomplicated and Complicated Pregnancies. By Icie G. Macy, Ph.D., Sc.D., and Harold C. Mack, M.D. Pp. 170, with tables and figures. Gratis to workers in either field. Children's Fund of Michigan, 660 Fredericks St., Detroit 2, 1952.

This volume is an excellent presentation of the use of the Tiselius apparatus in the electrophoretic determination of the various protein fragments in the blood plasma. As such, its value probably will be in the relative rather than the absolute. The apparatus is complicated, and more than ordinary skill is required in its successful use. The subjects and methods of study are succinctly set forth with the advantages and disadvantages of the procedure. This method will undoubtedly prove to be a valuable tool in the search for more precise data of the physiologic variability of the plasma proteins. It is very possible that only very general evaluation can be made of the electrophoretic determinations as shown in this volume and large numbers of comparable figures will be necessary. This volume of 170 pages closes with 120 pages of seriatim data obtained by electrophoresis of the blood plasma proteins in pregnancy in uncomplicated cases and in disease conditions.

Über Lageanomalien des Magendarmtractus infolge Störungen der fetalen Darmdrehung. By Max Grob. Price, 24 Swiss francs. Pp. 148, with 110 illustrations. Benno Schwabe & Co., Klosterberg 27, Basel 10, 1953.

The monograph delineates the normal development of the position of the intestine. In a chapter given on general considerations of position disorders, three main categories are distinguished: disturbances of rotation, disorders of growth of separate parts of the intestine, and

disorders of the attachment of the mesenteries. In other chapters, various abnormalities of rotation are described, including nonrotation, malrotation, and inverse rotation, as well as anomalies affecting various sections of the intestine. On the basis of 28 clinical observations in children from 1 day to 15 years of age, given in detail and with reference to the literature, the symptomatology is outlined. In the absence of symptoms referable to the abnormality, a diagnosis was made accidentally by a roentgen examination or at operation or at postmortem examination. In a number of cases additional disorders of development were noted, for instance, congenital heart lesions. Symptoms referable to the anomalies may be light and more chronic or acute and very severe. Most frequent are intestinal obstructions, torsion of the mesentery, and disorders of the circulation with their consequences. For further detail it is worth while to consult the monograph.

Immunity: Hypersensitivity, Serology. By Sidney Raffel, Sc.D., M.D. Price, $8. Pp. 531, with illustrations. Appleton-Century-Crofts, Inc., 35 W. 32d St., New York 1, 1953.

In this book, the author's approach has been to discuss all of the known phenomena related to the immunity to infection. As is pointed out, there are many factors besides humoral antibody immunity to consider, but none are as well studied or understood. However, in the book there is a review of much of what is known about these factors, as concerns both the virulence of the parasite and the defenses of the host. Since the major studies in the field of immunity have been concerned with antibody immunity, there is a logical extension into the fundamentals of serology and a review of pertinent material about antigens, antibodies, and complement and their interactions. Following this there are several chapters on the epidemiological aspects and effect of environmental factors on the several kinds of immunity discussed.

In the second section, other diseases related to antibodies in which the antibodies are not defense mechanisms but are involved in pathogenesis are discussed, as well as the relationship of hypersensitivity to immunity.

In the third section, there is a return to immunity. The resistance factors in nine bacterial and three virus diseases are discussed in detail.

The book ends with a return to serology in the form of discussion of antigens, microbial and cellular.

The style of the book is that of a rather extensive review of the literature with an occasional insertion of the author's opinions, mainly for the sake of clarity. In spite of the several major digressions, the material fits together well. The level of the book is such that it should be useful for medical students in a course in this field. It gives the practicing doctor who has not seriously considered these problems for several years an opportunity to catch up to within one to two years of the current literature in most subjects. In this latter use it should be particularly valuable.

The format is good, the tables are clear, and some of the diagrams, particularly those concerning antigen-antibody reactions, are quite lucid.

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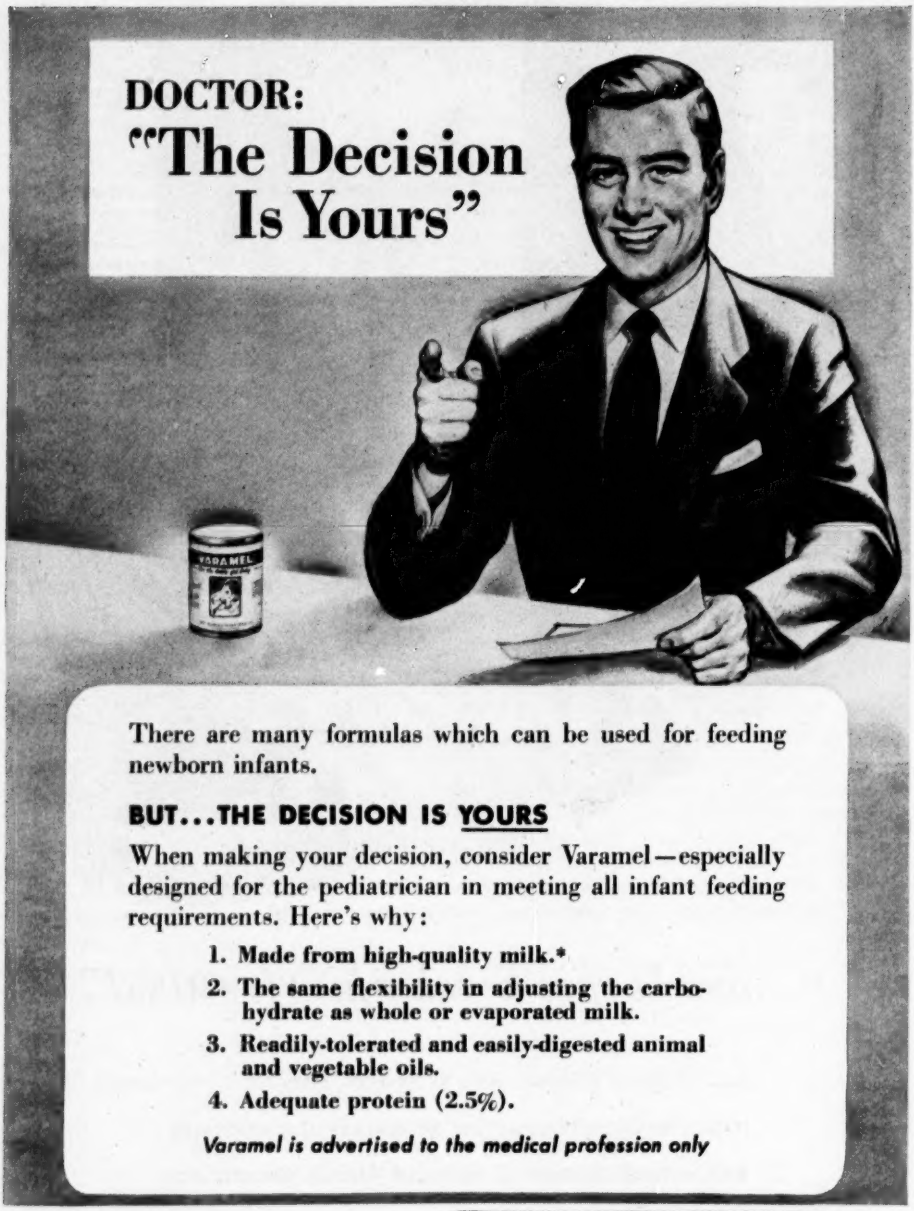

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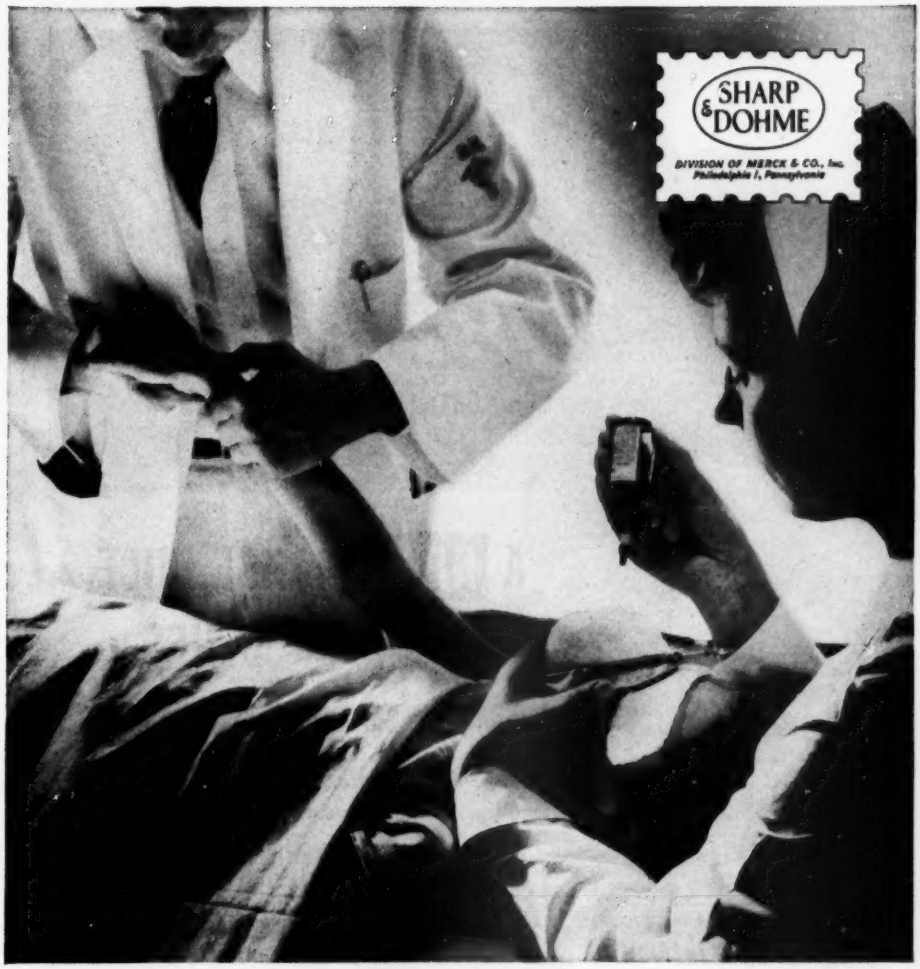

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Bibliography: 1. Vignec, A. J., and Mitty, V. C.: J. Pediat. *40*:576 (May) 1952. 2. Seidmon, E. E. P.: Am. J. Digest. Dis. *18*:274 (Sept.) 1951.

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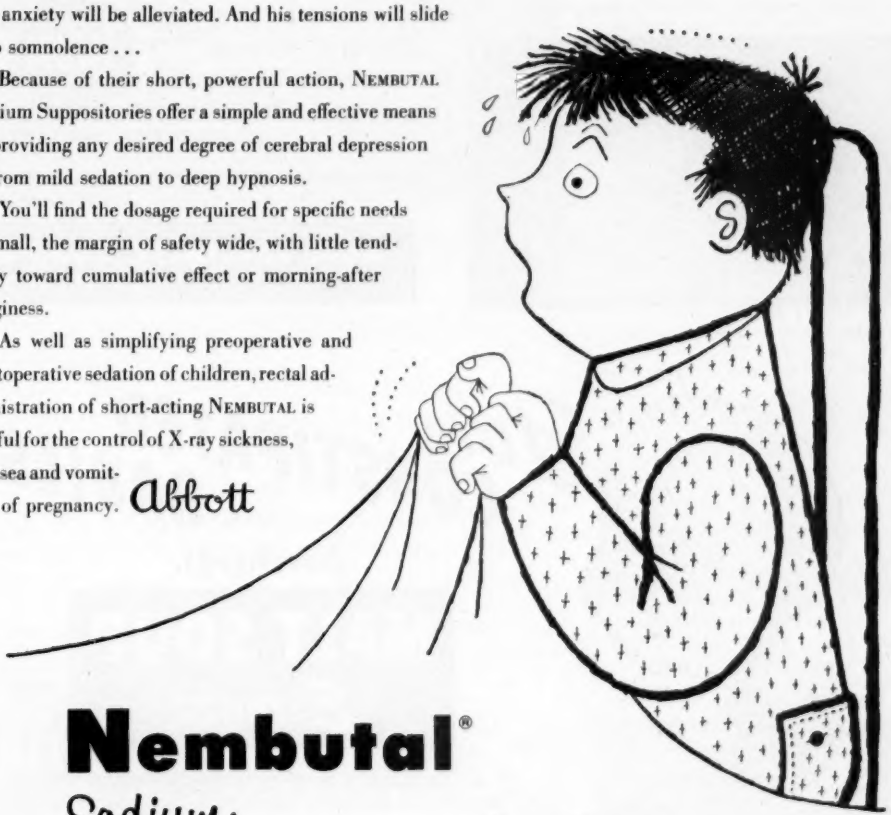

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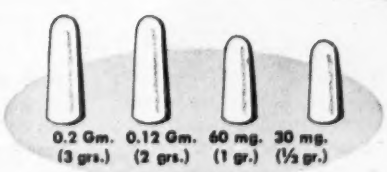

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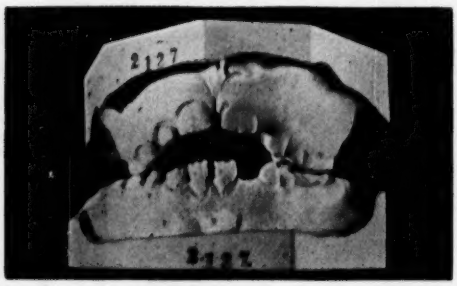

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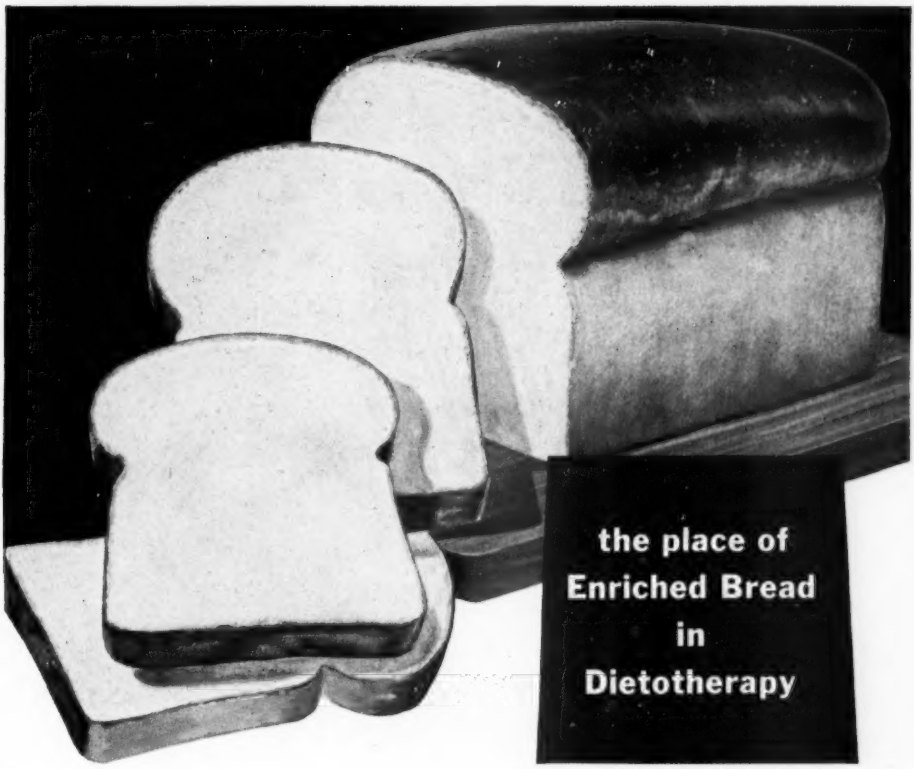

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